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13. ABSTRACT (Maximum 200) Implementation of a new predoctoral program in the "Biology of Breast Cancer" has facilitated the training of investigators committed to future careers in the study of breast cancer. The scope of this program has been limited to the training of predoctoral (i.e., Ph.D. and M.D., Ph.D.) candidates. USAMRDC support for this program has resulted in the development of a truly outstanding, multidisciplinary, didactic curriculum in tumor biology, which includes a strong emphasis in breast cancer. To date, 16 trainees have matriculated into this new training program. Two trainees have successfully completed this training program and have left the Mayo Clinic to continue their training/careers in breast cancer research. All of the remaining trainees are conducting breast cancer relevant thesis research and continue to make excellent progress in their studies. This final report includes the product of our last task (i.e., Task 6) of our original statement of work which is a formal written evaluation, and also includes the comments of our two external reviewers (see Appendix). The longer term continuation and success of this new training program has been assured by the recent (8/98) award of a new predoctoral training grant from the NCI (CA 75926).				
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FOREWORD

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Lita J. Mair
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Annual Report for DAMD 17-94-J-4116

August, 1998

Biology of Breast Cancer: A Predoctoral Training Program

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INTRODUCTION

This annual report covers activities for **DAMD 17-94-J-4116** entitled the "Biology of Breast Cancer: A Predoctoral Training Program" for the period September, 1997 through August, 1998, and also provides a cumulative summary of the activities of this new training program since its inception. In this report we present documentation for the successful completion of the past academic year, and the initiation of the 1998-1999 academic year.

The six tasks that were presented in the original application are listed, below:

- **Task 1:** Organize Biology of Breast Cancer Predoctoral Training Program Faculty and Curriculum.
- **Task 2:** Establish New Courses in Specialized Aspects of Tumor Biology, Emphasizing the Cell and Molecular Biology of Breast Cancer.
- **Task 3:** Establish Appropriate Mechanisms for Student Recruitment Into This New Training Program.
- **Task 4:** Implement the New Biology of Breast Cancer Predoctoral Training Program Curriculum.
- **Task 5:** Assess Student Progress.
- **Task 6:** Assess Biology of Breast Cancer Predoctoral Training Program Effectiveness and Formalize Assessment in a Written Report.

As noted in the written review of our last progress report (February 12, 1997), we had successfully completed all of these tasks except Task 6 at the time of our last report. Enclosed as a component of this final report (Appendix L) is the formal written self evaluation that was submitted to members of our External Advisory Committee (Drs. Bissell, King and Moses) in June, 1998. The comments of two of these external reviewers (Drs. Bissell and Moses) are also included in the Appendix (Appendices M, N).

BODY

Goals

The goals of the Biology of Breast Cancer (BBC) and Tumor Biology Training Program are four-fold:

- First, to provide trainees with a solid and uniquely multidisciplinary knowledge base in the biology of cancer using breast cancer as the paradigm.
- Second, to guide the development of each individual trainee so that they achieve their fullest academic and research potential.
- Third, to aid trainees in the establishment of their professional network of peers and colleagues in the field of breast cancer research.
- Fourth, to stimulate new working alliances between students, fellows, and staff participating in breast cancer research, education, and clinical endeavors at the Mayo Clinic and within the Mayo Cancer Center.

Overview

The "Biology of Breast Cancer" is a multidisciplinary predoctoral training program in the biology of cancer, with a specific emphasis on breast cancer. The focus of the program is to provide an educational environment that stimulates excellence in scientific thought and training while simultaneously providing exposure to all of the major fields of study relevant to tumor biology. While a defining feature of this program is its research focus and integral link with clinical aspects of breast cancer, a general foundation in tumor biology is both important and essential in achieving this goal. The curriculum for this program is outlined in the course syllabus material, provided below, and the thesis research topics of the students matriculating in the program. This information clearly details and substantiates the major breast cancer research focus of this new training program. Research and training are broadly focused on gene regulation, cell cycle control, cancer genetics, oncogene and tumor suppressor action, tumor immunology, signal transduction, antitumor pharmacology, with a particular emphasis on breast cancer, but also includes investigators with research programs in ovarian, uterine, lung, G.I., brain, and prostate cancers. Students participate in laboratory-based research, as well as in a formal tumor biology curriculum that integrates current concepts in cell growth control with the natural history of human tumors.

The Biology of Breast Cancer Training Program has been supported by extramural training grants since its inception. Currently, these training grants include an award from the US Army Medical Research and Materiel Command in the "Biology of Breast Cancer" (DAMD17-94-J-4116), and a T32 Training Grant from the National Cancer Institute in "Tumor Biology" (CA75926). In addition, the program operates under the generous support of the Mayo Foundation through the Mayo Graduate School and the Mayo Cancer Center. Individual trainees also have been successful in competition for individual research awards (see Appendix K).

Program Structure

Administrative Structure

The BBC training program is administrated through the Mayo Graduate School, and is closely allied with the Mayo Cancer Center. Day-to-day program administration operates largely through the Director (Dr. Salisbury) and Co-director (Dr. Maihle) of the Biology of Breast Cancer and Tumor Biology Training grants. Long range planning and administration operates through the Tumor Biology Education Committee (Drs. Salisbury, Maihle, Federspiel, Jelinek, and Tindall, and a trainee, Mr. J. Baines). The Education Committee meets each academic quarter to discuss student recruitment, student progress, and coordination within the Tumor Training Program curriculum. In addition, the directors of the three cancer-related pre- and postdoctoral training grants (Drs. Salisbury, Maihle, Getz, and David) and the Director of the Mayo Cancer Center (Dr. Prendergast) interact to coordinate ongoing programs and activities related to cancer research and education at Mayo in general. The Biology of Breast Cancer Training faculty also meet quarterly, in addition to frequent interactions through participation in program courses, journal clubs, research workshops, and a biweekly social hour called the "Tumor Biology Tea."

Qualifications of the Program Faculty

The BBC training faculty (see Appendix E for listing) consists of approximately 50 full and associate members drawn from each of the basic science departments, as well as clinical faculty who participate in scholastic activities of the program but who do not have active research laboratories. The level of individual faculty participation varies each year for specific courses, topics and journal clubs. Nonetheless, a growing and enthusiastic cadre of participating faculty has emerged. In future years the program may elect to restructure its faculty based on degree of faculty participation, given the mounting enthusiasm for this program, as well as recent and ongoing recruitment of new staff in the area of cancer biology. At this time, however, faculty privileges will remain as they are in order to promote both the inclusively and multidisciplinary nature of this new training program. While most individual faculty are associated with traditional discipline-based basic science and clinical departments (such as Oncology, Molecular Biology, Experimental Pathology, Pharmacology, etc.) the administrative structure of the Program is that of an interdisciplinary programmatic unit. This programmatic structure reflects the interdisciplinary nature of the major research and academic efforts of the associated faculty.

- Full members of the training faculty have an established track record of accomplishment in biomedical research as demonstrated by significant publications of high scientific merit, excellence, and innovation. Overall, the faculty have consistent records of extramural funding in support of their individual research programs.
- The collective interests of this training faculty are quite broad, but all show direct breast cancer relevance. These interests include: cell signaling, cancer genetics, gene regulation, tumor immunology, oncogene and tumor suppressor action, cell cycle regulation, tumor virology, gene therapy, hormonal regulation, and molecular cytology. Most training faculty are also members of the NCI-designated Mayo Cancer Center.
- Faculty drawn from both clinical and basic science departments contribute to the Training Program through participation in a variety of relevant educational activities and as clinical instructors. Faculty from outside the program may serve as advisory members of qualifying examination and thesis committees, however, they may not serve as research mentors for students in the Biology of Breast Cancer Training Program.

Program Curriculum

Introduction

The program curriculum and thesis research is a predoctoral training program leading to the Ph.D. degree in Biomedical Sciences. Each year, 3 to 5 students are accepted into the program for an appointment term of 4 to 5 years. The program strives to maintain a steady state level of 15 to 20 students. Trainee stipends initially are supported through institutional funds. Students qualify for support from extramural training grants (third through fifth year), following successful completion of the qualifying examination. The training program curriculum includes didactic course work, journal clubs, research seminars and workshops, and tutorial and special clinical activities. Students who matriculate into the program must meet the general course requirements of the Mayo Graduate School in which a minimum of 15 credits are required from the Graduate School Core Curriculum. Students must also complete 20 credits from the didactic Tumor Biology Program curriculum and the remainder of their credit requirements can be completed through elective courses offered by the Tumor Biology Program, the Mayo Graduate School or by special topics courses given at other institutions and sanctioned by the Mayo Graduate School. For students in the Biology of Breast Cancer Program these electives must include a course entitled "Biology of Breast Cancer" (see Appendix F for outlines of selected courses). A student's program of core courses is individually developed by the Education Committee in consultation with the student and his/her advisor.

Summary of the Curriculum:

Graduate School Core Offerings (15 Credits, minimum)

- Genome Biology (3)
- Immunology (3)
- Principles of Cell and Tissue Design (3)
- Biochemistry (3)
- Genetics (1)
- Pharmacology (2)
- Developmental Biology & Statistics (1)
- Biology of Disease (1)
- Ethics (1)

Required Biology of Breast Cancer Course Offerings (20 Credits)

- Tumor Biology I: Introduction to Tissue and Tumor Biology (3)
- Tumor Biology II: Origins of Human Cancer (3)
- Tumor Biology III: Growth Factors, Oncogenes, and Tumor Suppressors (3)
- Biology of Breast Cancer (1)
- Current Topics in Tumor Biology: Journal Club (1) x 3
- Research Seminars in Tumor Biology and Tumor Biology Interest Group (1)
- AACR Course in Histopathology of Cancer, Keystone CO. (1)
- Laboratory Rotations in Tumor Biology (3 required rotations, 2 credits each = 6 total)
- Research in Tumor Biology (Thesis Research (0))

Recommended Electives

- Quantitative Biology I-III, Neuroscience (1), Integrated Physiology (5)
- Tumor Immunology (1), Business of Science and the Science of Business (1)
- Cytogenetics (2)

Biology of Breast Cancer Track and Core Curriculum Schedule

Year I or II Fall Quarter	M	T	W	Th	F
9:00-10:00	Biochemistry	Immunology	Biochemistry	Immunology	Biochemistry
10:00-11:00	Genome Biology		Genome Biology		Genome Biology
11:00-12:30	Tumor Biology I		Tumor Biology Journal Club		Tumor Biology I

Year I or II Winter Quarter	M	T	W	Th	F
9:00-10:00	Cell Biology	Genetics	Cell Biology		Cell Biology
11:00-12:30	Tumor Biology II		Tumor Biology Journal Club		Tumor Biology II

Year I or II Spring Quarter	M	T	W	Th	F
9:00-10:00	Pharmacology		Pharmacology		Pathobiology
10:00-11:00			Development + BioStatistics		
11:00-12:30	Tumor Biology III		Tumor Biology Journal Club		Tumor Biology III

Core Courses	Tumor Biology Courses
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Additional advanced elective courses may be chosen in any area from the Mayo Graduate School Bulletin to fulfill the overall degree requirement of 35 credits. In addition, all students in the training program are required to take formal classes in Radiation Safety, Animal Care and Use, and also participate in an NIH Grant Writing Workshop. These required courses are not administrated by the Mayo Graduate School, and, therefore, are not offered for Graduate School credit.

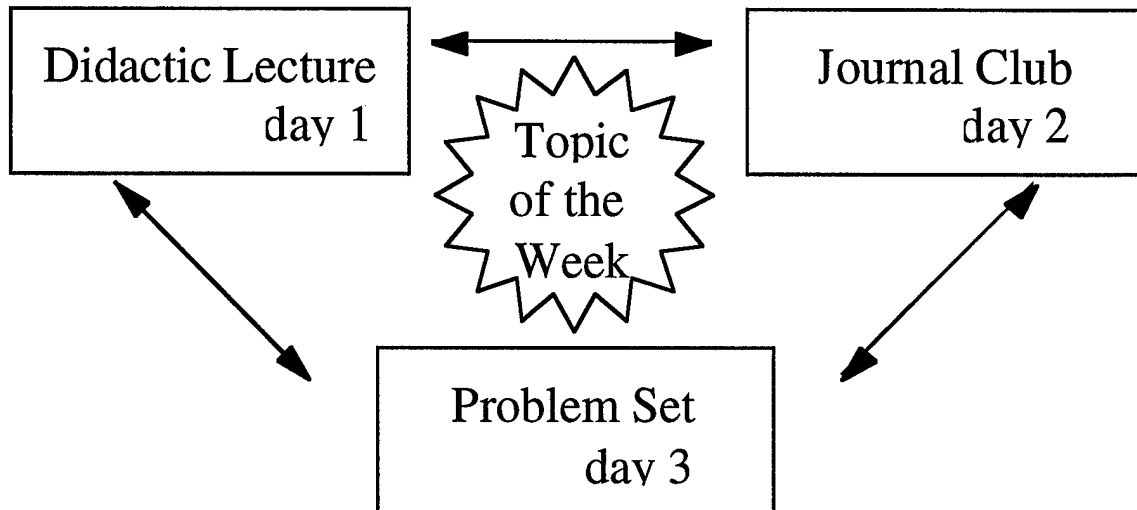
Program Implementation

Innovative Strategies for Teaching

Tumor Biology track courses establish a solid foundation in the biology of cancer. In practice, the biology of breast cancer is emphasized as an illustrative paradigm throughout the program curriculum. Issues of fundamental importance to understanding breast cancer are also relevant to other cancers, and the converse is also true. Likewise, there are many instances where the illustrating example of a relevant point may involve biological systems as diverse as yeast and frogs (not breast cancer research, but directly relevant to improving our understanding of breast cancer). Thereby, the tumor biology curriculum is grounded in basic cancer biology with the aim of leading students to a thorough understanding of all aspects at the forefront of breast cancer research. In order to accomplish this, our curriculum has been strategically developed to provide a strong foundation in the study of cancer using breast cancer as the model wherever possible. For example, to illustrate the significant emphasis on and integration of breast cancer in the overall curriculum, topics in breast cancer are featured in three 3 credit hour courses in the curriculum (see below), as well as in approximately one out of every three journal club presentations. Moreover, *all* trainees are required to register for a didactic course in "The Biology of Breast Cancer" (TBIO 8305, page 134 in the Mayo Graduate School Bulletin). The three major courses were organized and are taught using breast cancer as the principle paradigm for instruction and content: "Introduction to Tissue and Tumor Biology" (Tumor Biology I, TBIO 5000), "Origins of Human Cancer" (Tumor Biology II, TBIO 8000), and "Growth Factors, Oncogenes and Tumor Suppressors" (Tumor Biology III, TBIO 8005) (see course outlines in Appendix F).

Tumor Biology Track courses share several distinguishing features and innovative strategies for teaching which enhance learning and student/faculty participation.

- **Course Structure:** Tumor Biology I, II, and III are given as an integrated series during the first three consecutive quarters following matriculation. Individually, these courses meet three times per week (1 1/2 hour per session) with an overview and historical review of a selected topic(s) for the current week presented in a didactic lecture format during the first class session. This is followed by a student presentation of a current or historically relevant research paper(s) in the area of the week's topic during the second class session using the journal club format. Finally, a round table small group problem set discussion format is used to focus on questions and problems relevant to the week's topic during the third class session. The research paper presentation and problem set discussions are carefully organized in order to thoroughly integrate research topics relevant to the theme of the week. The effectiveness of these active learning/teaching strategies is apparent to all participants in these courses. The active involvement of students in the learning and discovery process, in information processing, and in the application of information to problems requires that students are accountable for learned information on an immediate and ongoing basis. Problem centered learning also puts learning into context and facilitates learning transfer. These sessions allow students to organize and categorize information into meaningful units and to 'discover' novel relationships and extract and assimilate important points in an interactive and participatory manner.



- **Balance of Historic and Current Scientific Perspectives:** Given the rapid pace of progress in the biological sciences and the exponential rate of growth of relevant literature the general philosophy that is promoted within the program is to *teach less better*. The objective here is to lay a strong foundation in cancer biology with the clear understanding that what is particularly relevant and important today, may not be so tomorrow. Therefore, emphasis is placed on developing effective learning skills, and the application of these skills to both historic paradigms, as well as critical review and evaluation of issues at the forefront of modern cancer biology.
- **Commitment, Accountability, and Responsibility:** Integral to the Tumor Biology Program teaching philosophy is *Peer Performance Assessment* and the *Team Learning Model*. These strategies create a climate in which all students are encouraged to grow. This results in a classroom environment where students from diverse backgrounds (including clinical fellows) feel welcome to fully participate in discussions and problem solving. In this way, desired student performances are tied directly to the efforts of the students themselves, to the involvement of students in the teaching-learning process, to the opportunities to make choices, and to the degree to which they interact with their peers and instructors. Emphasis is placed on organization and presentation skills, accountability tracking, and peer assessment and feedback. Our experience with this learning model is that trainees rapidly gain a level of professional expectation of their peers (and themselves) that both promotes and enhances the general level of academic and scholastic effort among trainees.
- **Continuing Education:** Senior students who have completed the formal didactic course requirements, and postdoctoral fellows who are supported by other cancer-related training grants actively participate in the journal club sessions that are an integral component of the Tumor Biology curriculum. In this way, senior trainees contribute to the critical mass of the class and also enhance the sophistication and the multidisciplinary nature of the discussions. Through this mechanism, more advanced trainees revisit current topics in cancer biology throughout their advanced training years. In this manner, advanced trainees have the opportunity to reinforce key concepts, to help new trainees better understand these concepts, and also to remain current with the rapid pace of development in the dynamic field of cancer biology. Likewise, Program faculty (and their laboratory personnel) actively participate in these regular weekly journal club sessions.
- **Integration of the Clinical Perspective:** The training program is designed to give the trainee a broad and well-rounded understanding of cancer from the basic science,

population science, and clinical perspectives. Integration of the clinical activities of the Mayo Cancer Center into the training program is achieved in several ways:

- ◇ First, clinical fellows and residents from a broad spectrum of cancer relevant programs (e.g., oncology, hem/onc, orthopedic research, gynecologic oncology, pediatric oncology, etc.) formally enroll and participate in training program courses and journal clubs. Active participation by clinical residents and fellows adds considerably to the multidisciplinary perspective of the student body, and to stimulating class discussions.
- ◇ Second, clinical staff give didactic lectures in areas of their specialty in Biology of Breast Cancer Training Program courses. For example in Tumor Biology II and III, individual lectures are given by clinical staff practicing in Surgery, Medical Oncology, Radiation Oncology, and Surgical Pathology.
- ◇ Third, program trainees are required to attend Mayo Cancer Center Research Workshops, Mayo Cancer Center Grand Rounds, and appropriate departmental, Research Society, Oncology Society and Hematology Society lectures, and receive course credit for participating in these activities (TBio 5101: "Research Seminars in Tumor Biology"). Students are made aware of relevant speakers through Email, direct mailings, and weekly announcements during the weekly journal club.
- ◇ The program curriculum is integrated with clinical practice wherever possible through special course related activities. For example, small group tours of the Surgical Pathology Suite (in TBio I) allow students to observe gross dissection of surgical specimens (including breast tumors), rapid freezing and cryomicrotomy, microscopic examination (via video monitors) and diagnosis by staff pathologists, and reporting to operating room surgeons. Additionally, Tumor Biology Program trainees are required to attend clinical rounds with a Mayo staff member (any division or department). Direct exposure to clinical activities such as these are useful for students to understand, based on first-hand observation, the intensity, dedication, and skill involved in the clinical care and treatment of cancer patients. These activities also promote the involvement of our clinical faculty in Biology of Breast Cancer Training Program activities.
- ◇ Finally, Tumor Biology trainees may have one or more clinical staff advisors participate as members of their Thesis Advisory Committee. Sometimes this involvement is fairly technical, e.g., participation by a Mayo Cancer Center biostatistician in study design and analysis. In other instances, however, clinical advisors may be directly involved in helping the trainee define a clinically relevant question, and/or assist them with tumor specimen acquisition and/or data analysis.

Additional Academic Activities

Seminars by Students, Faculty and Invited Speakers: Extensive institutional resources support seminars by nationally and internationally recognized scientists and clinicians on the Mayo Rochester campus. Approximately 350-400 speakers come to the Rochester campus each year. Trainees are, therefore, exposed to diverse biomedical research opportunities, and institutionally and departmentally-based research seminars throughout the year. In December of 1997, students of the Tumor Biology Program hosted Dr. Judah Folkman (Harvard University) who presented the Annual Findling Lecture of the Mayo Graduate School. The 1998-1999 academic year will feature a series of visiting speakers who will focus on the broad topic of Epigenetics and Cancer. During each of their research years, Tumor Biology Trainees also present research seminars and research posters in multidisciplinary research workshops and retreats (e.g., the Mayo Graduate School Annual Research Symposium, the Joint Mayo Cancer Center/Laboratory Medicine Retreat). More recently, we have formalized the Tumor Biology Interest Group (TBIG) for Mayo Graduate

School course credit. This monthly research workshop provides the opportunity for all Tumor Biology trainees (pre- and postdoctoral) to regularly present their research plans, proposals, and results in a constructively critical internal forum.

Attendance at National Research Meetings: All students are supported to attend at least one national scientific meeting each year even if they are not presenting an abstract. If they are presenting their work, attendance at additional meetings is encouraged and supported by the research mentor's laboratory. Mentors take an active role in introducing students to the professional culture and 'networking' critical to success in any biomedical research career through this mechanism. In recent years, Biology of Breast Cancer Training Program trainees have attended and presented at the following national meetings: AACR, ASCB, FASEB, Annual Oncogene Meetings, Annual Human Cancer Meeting, Cold Spring Harbor Cancer Genetics Meetings, Salk Tyrosine Phosphorylation Meetings, and various Gordon and Keystone Conferences (see Table IV, Appendix D).

Research Training

Selection of Thesis Laboratory, Mentor, and Thesis Committee Members: Trainees typically matriculate in June through August and are required to complete three laboratory-based (minimum 8 weeks each) rotations during their first year. Any laboratory-based Mayo Graduate School faculty member may serve as a mentor for these research rotations. Selection of the thesis mentor follows completion of successful laboratory-based rotations by mutual consent of the student and mentor with the sanction of the Training Program Education Committee and Mayo Graduate School Education Committee. The qualifying examination consists of a written thesis proposal, an oral presentation (TBIG forum), and its defense before a thesis committee consisting of a minimum of 4 faculty (including the thesis advisor), and when appropriate, an extramural committee member from outside the institution. Typically clinical or extramural committee members' research specialties are related to the general area of the student's thesis topic. Following successful completion of the qualifying examination, research progress is assessed through regular Thesis Advisory Committee meetings (minimum of one Thesis Advisory Committee meeting per year). While Thesis Advisory Committee members are available for advice, technical assistance, and consultation throughout the year, these meetings provide a formal opportunity for input by the Thesis Advisory Committee on progress and experimental aspects of the thesis project. The chair of the Thesis Advisory Committee formally reports the outcome of each committee meeting in writing to the Training Program Education Committee and to the Mayo Graduate School.

Thesis Research: The Biology of Breast Cancer Training Program places strong emphasis on thesis research. All laboratory-based faculty have demonstrated records of research training at both the predoctoral and postdoctoral levels. The specific details of an individual student's research training plan are developed following the selection of a thesis advisor and in consultation with the Thesis Advisory Committee. The thesis research project must be *hypothesis driven and experimental in nature* and must, in addition, have a *direct relevance to the biology of cancer*. For a listing of BBC trainees and their thesis titles, see Appendix B.

Ph.D. Thesis: The thesis is the most important document that the Ph.D. candidate prepares during the course of graduate study, and is a record of the scientific accomplishments that justify the awarding of the Ph.D. degree. The thesis is archival. Consequently, the Mayo Graduate School has developed standards for its format and style, and our trainees adhere to these guidelines. The thesis examination consists of a formal thesis research seminar open to all members of the Mayo community followed by a meeting with the Thesis Examining Committee

during which the scientific merit and accomplishments of the candidate are evaluated. Successful completion of a research thesis typically also results in two or more research manuscripts submitted for publication in peer-reviewed journals of high scientific standards.

Student Recruitment, Progress and Track Evaluation

Trainee Candidates: Students recruited into the Biology of Breast Cancer Training Program are selected on the basis of outstanding academic credentials, a stated desire to study and conduct research in the area of breast cancer biology, and an assessment of individual research potential by the training faculty (see Appendix A for table of BBC academic credentials). Many of the applicants to the Mayo Graduate School have had research experience within the Mayo system through summer undergraduate research internships. Typically, candidates for admission to Mayo's graduate programs apply directly to the Graduate School where their academic credentials, letters of recommendation, and personal statements are placed on record. Applicants are selected for on-site interview by the Mayo Graduate School Admissions Committee. The interview process involves faculty and student assessment of each applicant's research and academic interests. The Biology of Breast Cancer Training Program also has placed special emphasis on recruitment and training of under-represented minorities. Currently the predoctoral class consists of a total of 16 students, 3 of whom are minorities (19%, including one Native American, and two Hispanic students). A sample student recruitment advertisement is included in the Appendix of this report (Appendix I).

Trainee Evaluation

Trainee evaluation takes place at several levels and is assessed by comparison of established and objective data relating recruitment credentials, program completion, academic performance, placement, and ultimately career achievement.

- Academic performance of trainees, including coursework evaluation and consideration of reports from the trainee's Qualifying Exam and Thesis Advisory Committees.
- Successful completion of the degree program.
- Success in gaining competitive pre- and postdoctoral fellowships and/or extramural funding.
- Ultimately, the appointment of these trainees to independent research positions with evidence of ongoing research activities relevant to cancer biology.

Curriculum and Program Evaluation

Curriculum and Program evaluation includes the areas listed below, as well as additional areas defined by the External Review Committee:

- Ability to recruit and retain outstanding Ph.D. candidates.
- Course content and appropriateness to the biology of breast cancer.
- Thoroughness of didactic and formal training in the biology of cancer.
- Effectiveness of teaching and examining methods and procedures.
- Vitality and effectiveness of student/faculty interactions in the academic components of the program.
- Evidence of faculty mentorship and establishment of intramural and extramural professional networks.
- Scope and role of individual faculty participation in the Biology of Breast Cancer Training Program.

- Integration of the clinical perspective and understanding of physician and patient concerns in the diagnosis and treatment of cancer.
- Overall effectiveness of the Program Director, Co-Director, Education Committee, and of the Graduate School in administrating the Biology of Breast Cancer Training Program.

In addition to these standards to be used for self-evaluation, the Biology of Breast Cancer Training Program has successfully completed two rigorous external reviews, each of which has resulted in an extramural training award (i.e., the US Army Medical Research and Materiel Command award for predoctoral training in the "Biology of Breast Cancer" (DAMD17-94-J-4116), and a T32 Training Grant from the National Cancer Institute for predoctoral training in "Tumor Biology" (CA75926). One aspect of the USAMRMC predoctoral award is a requirement for formalization of an External Advisory Committee and periodic external review by this Committee. This formal written self evaluation and two external reviewers' comments (i.e., Dr. M. Bissell and Dr. H. Moses) are included as a component of the Appendix of this final progress report (Appendices L-N).

In addition, our experiences with the development and implementation of this new training program will be presented (poster format) at the 1998 American Association for Cancer Education Meeting to be held in Portland, Oregon (see Appendix O for abstract).

Syllabus Outlines for Selected Tumor Biology Track Courses

Mayo Tumor Biology track courses cover a series of topics of historic relevance and primary importance to cancer biology. In addition, each year course organization and content have evolved according to current trends and in order to incorporate breaking forefront issues in this dynamic field. Course syllabus outlines for 1997-1998, indicating topic, format, and faculty are included in the Appendix (Appendix F).

CONCLUSIONS

In the period 1994-1998 funding from the USAMRMC Breast Cancer Research Program was used to begin the implementation of a new multidisciplinary training program in the "Biology of Breast Cancer" at the Mayo Clinic in Rochester, Minnesota. The initiation of this new training program has resulted in the development of a new didactic curriculum in Tumor Biology with a special emphasis on breast cancer, a new journal club, and new working alliances among Mayo Clinic faculty interested in breast cancer research. To date, a total of sixteen students have matriculated into this training program, two of whom have successfully completed their training and have left the Mayo Clinic to continue their research training/careers in the field of breast cancer research. This new training program has recently completed formal internal and external reviews, and a copy of these reviews is included as a component of this final report. While the leaders of this program have identified future goals and objects to continue to enhance the quality of this new training program the overall consensus from these reviews is that this new program has been quite successful to date, and importantly, provides a truly outstanding foundation for the training of future generations of investigators dedicated to the field of breast cancer research. On behalf of all the participants in this new training program we express our sincere gratitude to the USAMRMC Breast Cancer Research Program for providing us with this opportunity.

REFERENCES - None.

DAMD 17-94-J-4116

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TABLE I. ACADEMIC CREDENTIALS OF TRAINEES

Name	Undergraduate School	GPA	GRE	TOEFL	Entry Date	Comments
Adelsman, Margaret	Bemidji State University, Bemidji, MN	3.85/4.0	630-V; 680-Q; 550-A=1,860	N/A	8/14/89	Ph.D. 5/17/96
Adrianne, Melissa*	California State University, Long Beach, CA	2.7/4.0	610-V; 580-Q; 590-A=1,780	N/A	7/21/98	
Baines, Jonathan*	University of Arizona, Tucson, AZ	3.39/4.0	MCAT screen score=64	N/A	6/3/96	
Canales, Nohelia*	Mount St. Mary's College, Los Angeles, CA	3.34/4.0	530-V; 550-Q; 610-A=1,690	N/A	1/6/97	
Calhoun, Eric	Truman State University, Kirksville, MO	3.65/4.0	490-V; 750-Q; 680-A=1,920	N/A	7/7/97	
Eley, Gregory	University of Georgia, Athens, GA	3.01/4.0	500-V; 780-Q; 790-A=2,070	N/A	7/1/96	
Faupel, Jessica	Gettysburg College, Gettysburg, PA	3.3/4.3	510-V; 630-Q; 730-A=1,870	N/A	8/3/98	
Holmen, Sheri	Western Michigan University, Kalamazoo, MI	3.56/4.0	390-V; 660-Q; 580-A=1,630	N/A	9/5/95	
Johnson, Julie	University of Wisconsin, Madison, WI	3.38/4.0	480-V; 720-Q; 680-A=1,880	N/A	7/8/96	
Lomberk, Gwen	Boston College, Chestnut Hill, MA	3.3/4.0	600-V; 710-Q; 790-A=2,100	N/A	9/8/97	
Myers, Shannon	Southwestern University, Georgetown, TX	3.8/4.0	590-V; 710-Q; 640-A=1,940	N/A	6/1/98	
Ritland, Steve	University of Wisconsin, Eau Claire, WI	3.54/4.0	610-V; 680-Q; 720-A=2,010	N/A	7/1/98	Ph.D. 7/10/98
Rogers, Michael	Brigham Young University, Provo, UT	3.66/4.0	790-V; 800-Q; 800-A=2,390	N/A	8/16/96	
Schehl, Colleen	University of Dayton, Dayton, OH (Bach.) Oklahoma State University, Stillwater, OK (M.S.)	3.3/4.0	600-V; 710-Q; 670-A=1,980	N/A	8/5/97	
Walters, Denise	McMaster University, Hamilton, Ontario, Canada	10.6/12	540-V; 640-Q; 650-A=1,830	N/A	6/1/98	
Xu, Kun	Beijing Medical University, Beijing, P.R. China	3.6	640-V; 780-Q; 740-A=2,160	630	6/18/97	

Maible, N.J.
Appendix A

*Members of underrepresented minority groups.

Table II: Trainees, Mentors, Thesis Titles

<u>Student</u>	<u>Mentor</u>	<u>Proposed Thesis Title</u>
Adelsman, M. A.	Dr. N. J. Maible	"Ligand-Independent Dimerization of <i>c-erbB1</i> Oncogenic v- <i>erbB</i> Products"
Baines, J. E.	Dr. D. H. Persing	"Novel Immunotherapeutic Approaches to Cervical Cancer"
Calhoun, E. S.	Dr. D. F. Jelinek	Thesis project not determined
Canales, N. D.	Dr. S. J. Gendler	Thesis project not determined
Eley, G. D.	Dr. C. D. James	"Characterization of the Epidermal Growth Factor Receptor Amplicon in Human Glioblastoma"
Holmen, S. L.	Dr. M. J. Federspiel	"Viral Receptors Engineered to Inhibit Viral Entry"
Johnson, J. L.	Dr. N. J. Maible	"Mechanisms of <i>c-erbB1</i> Oncogenic Signaling"
Lomberg, G.	Dr. D. I. Smith	Thesis project not determined
Ritland, S. R.	Dr. S. J. Gendler	"Genetic Linkage for Tumor Modifier Loci in the MMTV-neu Transgenic Mouse Mammary Tumor Model"
Rogers, M. S.	Dr. E. E. Strehler	"Studies on the Structure and Function of Human CLP in Breast Cancer"
Schehl, C. M.	Dr. F. Couch	"The Role of BRCA1/2 Mutations in Breast Cancer"
Xu, K.	Dr. F. Prendergast	"Molecular Studies of Farnesyl Transferase Inhibitors"
Adriance, M.	Rotations	N.A.
Faupel, J.	Rotations	N.A.
Myers, S.	Rotations	N.A.
Walters, D.	Rotations	N.A.

TABLE III. PUBLICATIONS OF TRAINEES

Appendix C

Adelsman, Margaret A.

Papers

Adelsman MA, Huntley BK, Maihle NJ: Ligand-independent dimerization of oncogenic *v-erbB* products involves covalent interactions. *J Virol* 70:2533-2544, 1996.

Adriance, Melissa

Abstracts

Adriance M, Garay P, Klig LS: Utilization and uptake of inositol in *Cryptococcus neoformans*. Southern California Branch of the American Society for Microbiology 60th Annual Meeting, San Diego, CA, 1996.

Adriance M, Hueston J, Garay P, Klig LS: Inositol transport and protein kinase C in *Cryptococcus neoformans*. CSULB 1997 Honor's in Science Student Research symposium, HHMI/MARC/MBRS, California State University, Long Beach, CA, 1997.

Adriance M, Garay P, Klig LS: Inositol utilization and transport in *Cryptococcus neoformans*. Graduate Women in Science, Sigma Chapter, Eighth Science Conference, Chapman University, Orange, CA, 1997.

Adriance M, Hueston J, Garay P, Klig LS: Regulation of inositol metabolism and the protein kinase C gene in *Cryptococcus neoformans*. American Society for Microbiology 97th General Meeting, Miami, FL, 1997.

Garay P, Adriance M, Klig LS: Examination of inositol transport and intercellular pools in *Cryptococcus neoformans*, American Society for Microbiology 98th General Meeting, Atlanta, GA, 1998 (submitted).

Canales, Nohelia

Abstracts

Bower A, Serdoncillo C, Canales N: The specificity of atrial natriuretic peptide on the release control of melanocyte stimulating hormone from the pituitary.

Canales N, Radice G: Histological analysis of mammary glands in P-cadherin deficient mice.

Bower A, Canales N, Becker K, Ocampo M: Atrial natriuretic peptide release inhibition by dopamine and melanocyte stimulating hormone.

Eley, Gregory

Papers

Eley G, Frederick L, Wang X-Y, Smith D, James CD: 3' end structure and rearrangements of EGFR in glioblastomas. *Genes, Chromosomes, and Cancer*, in press, 1998.

Abstracts

Eley G, Frederick L, Wang X-Y., Smith D, James CD: Genomic characterization of EGFR rearrangements resulting in C-terminal truncations in glioblastomas. American Association for Cancer Research Annual Meeting, New Orleans, LA, March 28-April 1, 1998.

Holmen, Sheri L.

Papers

Holmen SL, Ginsberg LC: Luciferase as a reporter gene for the expression of glucose 6-phosphate dehydrogenase in mammalian cells. *Proceedings, Eighth National Conference on Undergraduate Research*, Vol. III, pp 923-927, 1994.

Holmen SL, VanBrocklin MW, Eversole RR, Stapleton SR, Ginsberg LC: Efficient lipid-mediated transfection of DNA into primary rat hepatocytes. *In Vitro Cell Dev Biol* 30:347-351, 1995.

Abstracts

Effect of insulin on glucose-6-phosphate dehydrogenase activity. Fourth Annual Undergraduate Research Symposium, Argonne National Laboratories, Argonne, Illinois, 1993.

Holmen SL, Ginsberg LC, Stapleton SR, Rank KB: Luciferase as a reporter gene for the expression of glucose-6-phosphate dehydrogenase in mammalian cells. National Undergraduate Research Conference, Western Michigan University, Kalamazoo, Michigan, 1994.

Soluble forms of the avian leukosis virus receptor Tv-a significantly inhibit virus infection in vitro and in vivo. Retrovirus Meeting, Cold Spring Harbor, New York, 1997.

Holmen SL, Schaefer-Klein JL, Payne WS, Dodgson JB, Federspiel MJ: Viral receptors and envelope glycoproteins engineered to inhibit viral entry. Retrovirus Meeting, Cold Spring Harbor, New York, p 45, 1998.

Johnson, Julie L.

Papers

Johnson JL, Fenton S, Sheffield LG: Prolactin inhibits epidermal growth factor-induced Ras-MAPK signaling in mammary epithelial cells. *J Biol Chem* 271:21574-21578, 1996.

Abstracts

Johnson JL, Fenton SE, Sheffield LG: The effect of prolactin on EGF-induced Ras activity in mammary epithelium. Experimental Biology Meeting, 1995.

Johnson JL, Jelinek D: Analysis of insulin-like growth factor expression on normal vs. transformed B cells. Mayo Graduate School Poster Session, 1996.

Johnson JL, Maihle NJ: Receptor-mediated endocytosis and v-erbB-mediated transformation. Experimental Pathology and Laboratory Medicine Symposia, 1997.

Lomberg, Gwen

Papers

Huang H, Reed CP, Mordi A, Lomberg G, Wang L, Shirdhar V, Hartmann L, Jenkins R, Smith DI. Frequent deletions within FRA7G at 7q31.2 in invasive epithelial ovarian carcinomas. *Genes, Chromosomes, and Cancer*, in press, 1998.

Ritland, Steve R.

Papers

Herrmann M, Hay I, Bartelt D, Ritland S, Dahl R, Grant C, Jenkins R: Cytogenetic and molecular genetic studies of follicular and papillary thyroid cancers. *J Clin Invest* 88:1596-1604, 1991.

- Ransom D, **Ritland S**, Kimmel D, Moertel C, Dahl R, Scheithauer B, Kelly P, Jenkins R: Cytogenetic and loss of heterozygosity studies in ependymomas, pilocytic astrocytomas, and oligodendrogliomas. *Genes Chromosom Cancer* 5:348-356, 1992.
- Ransom D, **Ritland S**, Moertel C, Dahl R, O'Fallon J, Scheithauer B, Kimmel D, Kelly P, Olopade O, Diaz M, Jenkins R: Correlation of cytogenetic analysis and loss of heterozygosity studies in human diffuse astrocytomas and mixed oligo-astrocytomas. *Genes Chromosom Cancer* 5:357-374, 1992.
- Cliby W, **Ritland S**, Hartmann L, Dodson M, Halling K, Keeney G, Podratz K, Jenkins R: Human epithelial ovarian cancer allelotype. *Cancer Res* 53:2393-2398, 1993.
- Cliby W, Sarkar G, **Ritland S**, Hartmann L, Podratz K, Jenkins R: Absence of prohibitin gene mutations in human epithelial ovarian tumors. *Gynecol Oncol* 50:34-37, 1993.
- Dodson M, Hartmann L, Cliby W, DeLacey K, Keeney G, **Ritland S**, Su J, Podratz K, Jenkins R: Comparison of loss of heterozygosity patterns in invasive low grade and high grade epithelial ovarian carcinomas. *Cancer Res* 53:4456-60, 1993.
- Tomlinson F, Keelan P, Scheithauer B, **Ritland S**, Jenkins R, Parisi J, Cunningham J, Olsen K: Aggressive medulloblastoma with high level n-myc amplification and p53 point mutation. *Mayo Clin Proc* 69:359-365, 1994.
- Cheng T, Ganju V, **Ritland S**, Sarkar G, Jenkins R: Analysis of p53 mutations in human gliomas by RNA single-strand conformational polymorphism. IN PCR in Neuroscience (G Sarkar, ed), pp 210-227, 1995.
- Dalrymple SJ, Herath JF, **Ritland SR**, Moertel CA, Jenkins RB: Use of fluorescence *in situ* hybridization (FISH) to detect loss of chromosome 10 in astrocytomas. *J Neurosurg* 83:316-323, 1995.
- Ritland SR**, Ganju V, Jenkins RB: Region-specific loss of heterozygosity on chromosome 19 is related to morphologic type of glioma. *Genes Chromosom Cancer* 12:277-282, 1995.
- Takahashi S, Shan AL, **Ritland SR**, Delacey KA, Bostwick DG, Lieber MM, Thibodeau SN, Jenkins RB: Frequent loss of heterozygosity at 7q31.1 in primary prostate cancer is associated with tumor aggressiveness and progression. *Cancer Res* 55:4114-4119, 1995.
- Ritland SR**, Rowse GJ, Chang Y, Gendler SJ: Loss of heterozygosity analysis in primary mammary tumors and lung metastases of MMTV-MTA_g and MMTV-neu transgenic mice. *Cancer Res* 57:3520-3525, 1997.
- Rowse GJ, **Ritland SR**, Gendler SJ: Genetic modulation of *Neu* proto-oncogene-induced mammary tumorigenesis. *Cancer Res* 58:2675-2679, 1998.
- Ritland SR**, Leighton JA, Hirsch RE, Morrow JD, Gendler SJ: Evaluation of 5-ASA for cancer chemoprevention: Absence of efficacy against adenomatous polyps in the Apc^{Min} mouse. Submitted, 1998.
- Ritland SR**, Rowse GJ, Weaver AL, Chang Y, Gendler SJ: Genetic mapping of mammary tumor modified loci in the MMTV-*neu* transgenic mouse. Submitted, 1998.
- Abstracts**
- Ritland S**, Cheng C: Selection of pumpkin genomic DNA clones by zinc finger gene homology screening. Wisconsin Academy of Sciences, Green Bay, Wisconsin, May 1988.
- Ransom D, Jenkins R, Olopade F, Diaz M, **Ritland S**, Bren G: Loss of chromosome 10 alleles and loss of α -interferon genes in human gliomas. (AACR, 1990) *Cancer Res Proc* 31:38, 1990.

- Ransom D, **Ritland S**, Jenkins R, Scheithauer B, Kelly P, Kimmel D: Loss of heterozygosity studies in human gliomas. (AACR, 1991) *Cancer Res Proc* 32:302, 1991.
- Jenkins R, Kimmel D, Moertel C, Stalboerger P, **Ritland S**, Ransom D. Cytogenetic and molecular genetic loss-of-heterozygosity studies in human ependymomas and pilocytic astrocytomas. (HGM11, 1991) *Cytogenet Cell Genet* 58:2029, 1991.
- Jenkins R, Ransom D, **Ritland S**, Moertel C, Dahl R, O'Fallon J, Scheithauer B, Kelly P, Kimmel D: Correlation of cytogenetics and loss of heterozygosity studies of chromosome 10 in gliomas. (4th International Workshop on Chromosomes in Solid Tumors, 1991) *Cancer Genet Cytogenet* 59:107, 1992.
- Herrmann M, **Ritland S**, Hay I, Jenkins R: Loss of heterozygosity studies in thyroid neoplasia. (4th International Workshop on Chromosomes in Solid Tumors, 1991) *Cancer Genet Cytogenet* 59:107, 1992.
- Cliby W, **Ritland S**, Hartmann L, Persons D, Podratz K, Jenkins R: Frequent allelic loss in epithelial ovarian cancers mapped to chromosome arms 6p, 6q, 11p, 13q, 17p, and 17q. (AACR, 1992) *Cancer Res Proc* 33:379, 1992.
- Wu P, **Ritland S**, Goellner J, Grant C, Jenkins R, Hay I: Allelic loss in differentiated non-medullary thyroid neoplasm. European Thyroid Association, 1992.
- Cliby W, **Ritland S**, Hartmann L, Dodson M, Podratz K, Jenkins R: Allelotype for epithelial ovarian cancer. Society of Gynecologic Oncologists, Palm Desert, California, February 1993.
- Dodson M, **Ritland S**, Cliby W, Podratz K, Hartmann L, Jenkins R: Loss of heterozygosity in low grade epithelial ovarian tumors. (AACR, 1993) *Cancer Res Proc* 34:511, 1993.
- Jenkins R, **Ritland S**, Halling K, Thibodeau S: An evaluation of microsatellite repeat expansion in human gliomas. Tenth International Conference on Brain Tumor Research and Therapy, Stalheim, Norway, May 1993.
- Jenkins R, Dodson M, Delacey K, **Ritland S**, Bartelt D, Cliby W, Podratz K, Hartmann L: Genetic studies of low and high grade epithelial ovarian tumors. 4th International Gynecologic Cancer Society, Stockholm, Sweden, August 1993.
- Dodson M, Hartmann L, Cliby W, DeLacey K, Keeney G, **Ritland S**, Su J, Podratz K, Jenkins R: Comparison of loss of heterozygosity patterns in invasive low grade and high grade epithelial ovarian carcinomas. Society of Gynecologic Oncologists, Orlando, Florida, February 1994.
- Dalrymple S, Herath J, **Ritland S**, Borell T, Jenkins R: Use of fluorescent in situ hybridization (FISH) to detect chromosome 10 loss in glial neoplasms. (Am Assoc Neurol Surgeons, 1993) *J Neurosurg* 80:413A, 1994.
- Ritland S**, Jenkins R: Deletion mapping of chromosome 19 in human oligodendroglioma, astrocytoma, and mixed oligoastrocytoma. (Keystone Tumor Suppressor Gene Symposia, Taos, New Mexico, February 1994) *J Cell Biochem* 18C:197, 1994.
- Ritland S**, Jenkins R: Quantitative image processing techniques in molecular genetic analysis. Keystone Histopathobiology of Neoplasia Workshop, Keystone, Colorado, July 1994.
- Ritland S**, Gendler S: Genetic analysis of tumorigenesis in transgenic mice. Mayo Dept. BMB Retreat, Winona, Minnesota, September 1995.
- Ritland S**, Rowse G, Gendler S: Loss of heterozygosity analysis in primary mammary tumors and lung metastases of mice transgenic for the polyoma middle T antigen. Genetic Mechanisms of Cancer, M.D. Anderson Cancer Center, Houston, Texas, October 1995.
- Ritland S**, Rowse G, Gendler S: Genetic analysis of APC^{Min} and MMTV-MTAg transgenic mice. Tumor Susceptibility Genes, Keystone Conference, February 1996.

- Rowse G, Ritland S, Gendler S: Genetic modulation of mammary tumor development in mice transgenic for the *neu* protooncogene. American Association for Cancer Research, San Diego, California, May 1997.
- Ritland S, Gendler S: Chemoprevention trials using 5-ASA in the Apc-Min mouse. Mayo Comprehensive Cancer Center, June 1997.
- Rowse G, Ritland S, Gendler S: Genetic modulation of mammary tumor development in mice transgenic for the *neu* protooncogene. American Association for Cancer Research, San Diego, California, May 1997.
- Rowse G, Ritland S, Gendler S: Role of genetic modulation in mammary tumorigenesis induced by overexpression of the *neu* proto-oncogene in transgenic mice. The Mouse in Mammary Carcinogenesis Research Meeting, Bar Harbor, Maine, September 1997.
- Ritland S, Gendler S: Cancer chemoprevention studies using piroxicam in the Apc^{Min} mouse. 5th International Conference on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Related Diseases, La Jolla, California, September 1997.
- Ritland S, Gendler S: Evaluation of 5-aminosalicylic acid for intestinal tumor chemoprevention in the Apc^{Min} mouse. 5th International Conference on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Related Diseases, La Jolla, California, September 1997.
- Ritland S, Rowse G, Chang Y, Gendler S: Genetic mapping of a tumor suppressor gene locus in MMTV-*neu* transgenic mice. AACR Tumor Suppressor Genes Special Conference, Victoria B.C., September 1997.
- Ritland S, Rowse G, Chang Y, Gendler S: Genetic analysis of mammary tumor susceptibility in MMTV-*neu* transgenic mice. DOD Era of Hope conference, Washington, D.C., November 1997.

Rogers, Michael S.

Papers

- Rogers MS: The overexpression of human cytosolic thymidine kinase in *E. coli*. Honors Thesis, Brigham Young University, Provo, UT, 1993.
- Borrowman A, Rogers MS, O'Neill KL: An improved washing apparatus for nucleoside phosphorylation assays. *BioTechniques* 15:402-406, 1993.
- Rogers MS, Strehler EE: Calmodulin. IN Guidebook to the Calcium-Binding Proteins (Celio MR, Pauls T, Schwaller B, eds), Oxford University Press, Oxford, UK, pp 34-40, 1996.
- Rogers MS, Strehler EE: Calmodulin-like proteins. IN Guidebook to the Calcium-Binding Proteins (Celio MR, Pauls T, Schwaller B, eds), Oxford University Press, Oxford, UK, pp 41-43, 1996.
- Garamszegi N, Garamszegi ZP, Rogers MS, DeMarco SJ, Strehler EE: Application of a chimeric green fluorescent protein to study protein-protein interactions. *BioTechniques* 23:864-872, 1997.
- Qian H, Rogers MS, Schleucher J, Edlund U, Strehler EE, Sethson I: Sequential assignments of ¹H, ¹⁵N, ¹³C resonances and secondary structure of human calmodulin like protein determined by NMR spectroscopy. *Protein Science*, 1998 (in press)

Abstracts

- Rogers MS, Leavitt RW, O'Neill KL: The overexpression of human cytosolic thymidine kinase in *E. coli*. Intermountain Branch Meeting of the American Society for Microbiology, May 1, 1993.

Rogers MS, Rhyner JA, Strehler EE: Identification and partial purification of a potential calmodulin-like protein specific target. Histopathobiology of Neoplasia Workshop of the American Association for Cancer Research, July 11, 1995.

Rogers MS, Rhyner JA, Strehler EE: Identification and partial purification of a potential calmodulin-like protein specific target. Annual Retreat of the Department of Biochemistry and Molecular Biology, Mayo Graduate School, July 22-23, 1995.

Rogers MS, Foley MA, Ziesmer SC, Roche PC, Hartmann LC, Strehler EE: Distribution of human calmodulin-like protein (CLP) in normal and tumor human tissue. The Department of Laboratory Medicine/Pathology and the Mayo Cancer Center Research Symposium, May 20, 1997.

Schehl, Colleen M.

Papers

Schehl CM, Ostrander GK: Identification of the *BRCA1* germline mutation, 797delAA, in a Japanese breast-ovarian cancer patient. *J Natl Cancer Inst* 89:1547-1548, 1997.

Schehl CM, Ostrander GK: Lack of germline mutations indicates the retinoblastoma (*Rb*) gene is not involved in hereditary predisposition to ovarian cancer in Japanese women. *Gynecol Oncol*, in press, 1998.

Abstracts

Schehl CM, Suzuki Y, Ostrander GK: Retinoblastoma (*Rb*) gene sequence mutations and predisposition to ovarian cancer in Japanese women. 88th Annual Meeting of the American Association for Cancer Research Annual Meeting, San Diego, California, April 12-16, 1997.

TABLE IV. MEETINGS/COURSES ATTENDED BY TRAINEES

Adelsman, Margaret

Histopathobiology of Neoplasia Workshop, American Association for Cancer Research, Keystone, CO, 1995.

Canales, Nohelia

Molecular Biology and Pathology of Neoplasia, American Association for Cancer Research, Keystone, CO, July 12-19, 1998.

Gregory Eley

Advanced Genome Sequence Analysis, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, March 18-31, 1998.

Molecular Biology and Pathology of Neoplasia, American Association for Cancer Research, Keystone, CO, July 12-19, 1998.

39th Annual Short Course in Medical and Experimental Mammalian Genetics, The Jackson Laboratory, Bar Harbor, ME, July 19-31, 1998.

Julie Johnson

Experimental Pathology and Laboratory Medicine Symposia, 1997.

American Association for Cancer Research Annual Meeting, New Orleans, LA, March 28-April 1, 1998

Molecular Biology and Pathology of Neoplasia, American Association for Cancer Research, Keystone, CO, July 12-19, 1998.

Lomberg, Gwen

Molecular Biology and Pathology of Neoplasia, American Association for Cancer Research, Keystone, CO, July 12-19, 1998.

Rogers, Michael

Histopathobiology of Neoplasia Workshop, American Association for Cancer Research, Keystone, CO, 1995.

American Association for Cancer Research Annual Meeting, New Orleans, LA, March 28-April 1, 1998

Colleen Schehl

Molecular Biology and Pathology of Neoplasia, American Association for Cancer Research, Keystone, CO, July 12-19, 1998.

Appendix E

THE FACULTY AND THEIR RESEARCH

Tumor Biology Program

- Robert T. Abraham, Associate Professor; Ph.D., Pittsburgh, 1981. Signal transduction; cell-cycle regulation; leukemogenesis.
- Matthew M. Ames, Professor; Ph.D., California, San Francisco, 1976. Development and characterization of novel antitumor agents.
- Amy G. Andrews, Assistant Professor; D.V.M., Michigan State, 1987. Animal models in cancer studies.
- Margot P. Cleary, Visiting Scientist; Ph.D., Columbia, 1976. Breast cancer; obesity; nutrition.
- Fergus J. Couch, Assistant Professor; Ph.D., University College Cork, Ireland, 1992. Identification and characterization of genes involved in familial and sporadic breast and ovarian cancer development. Functional analysis of the BRCA2 breast and ovarian cancer predisposition gene.
- Chella S. David, Professor; Ph.D., Iowa State, 1966. Immunogenetic aspects of immune response, with emphasis on the major histocompatibility complex class II Ia genes and T-cell receptor gene.
- Gordon W. Dewald, Professor; Ph.D., North Dakota, 1972. Cytogenetics and molecular cytogenetics of congenital disorders and hematologic malignancies.
- Richard L. Ehman, Professor; M.D., Saskatchewan, 1979. Magnetic resonance imaging.
- Charles Erlichman, Professor; M.D., Toronto (Canada), 1974. Pharmacology of drugs used in cancer therapy.
- Mark J. Federspiel, Assistant Professor; Ph.D., Michigan State, 1987. Retroviral vectors; antiviral strategies; molecular medicine.
- Lorraine A. Fitzpatrick, Professor; M.D., Chicago, 1980. Prostate cancer metastatic to bone; skeletal calcification; steroid regulation of metastatic disease.
- *Sandra J. Gendler, Associate Professor; Ph.D., USC, 1984. Tumor cell biology; mucins in cancer and cystic fibrosis.
- Michael J. Getz, Professor; Ph.D., Texas at Houston, 1972. Molecular biology of peptide growth factors; biology of tissue factor in tumorigenesis.
- Joseph P. Grande, Associate Professor; Ph.D., 1983, M.D., 1985, Chicago. Extracellular matrix and breast cancer; tumor pathology.
- James N. Ingle, Professor; M.D., Johns Hopkins, 1971. Clinical trials, hormonal therapy, and prognostic/predictive factors in breast cancer.
- C. David James, Associate Professor; Ph.D., Wright State, 1986. Cancer genetics; cell cycle regulation.
- Diane F. Jelinek, Assistant Professor; Ph.D., Texas Southwestern Medical Center, 1985. Cytokine-mediated signaling and gene expression in normal and malignant human B lymphocytes.
- Robert B. Jenkins, Associate Professor; Ph.D., 1981, M.D., 1983, Chicago. Genetics of brain, prostate and women's cancer.
- Larry M. Karnitz, Assistant Professor; Ph.D., Iowa, 1989. Signaling mechanisms of oncogenes and hemopoietic growth factors; molecular radiobiology.
- Scott H. Kaufmann, Associate Professor; M.D./Ph.D., Johns Hopkins, 1981. Pharmacology of topoisomerase-directed antineoplastic agents; apoptosis; resistance to anticancer drugs.
- Paul J. Leibson, Associate Professor; Ph.D., 1981, M.D., 1979, Chicago. Tumor immunology; lymphocyte activation; antiviral immunity.
- Vanda A. Lennon, Professor; M.B.B.S., Sydney (Australia), 1966; Ph.D., Melbourne (Australia), 1973. Immunobiology of autoimmunity and cancer; ionic channel protein antigens in human neoplasms of lung, ovary, and breast (carcinomas), and thymic epithelium (thymoma).
- Edward B. Leof, Associate Professor; Ph.D., North Carolina, 1982. Regulation of cellular proliferation; genetics of pneumocystis carinii.
- Ricardo V. Lloyd, Professor; M.D./Ph.D., Wisconsin, Madison, 1975. Endocrine tumor biology, especially pituitary and thyroid.

- John A. Lust, Assistant Professor; M.D./Ph.D., Boston University, 1983. Role of IL-6 and IL-6R in pathogenesis of multiple myeloma; detection of minimal residual disease in myeloma transplant patients by PCR.
- L. James Maher, Associate Professor; Ph.D., Wisconsin, 1988. Nucleic acid biochemistry; triple helix DNA.
- Nita J. Maihle, Associate Professor; Ph.D., Yeshiva (Einstein), 1983. Molecular basis of cancer; human breast, ovarian, and prostate carcinomas; gliomas.
- David J. McKean, Professor; Ph.D., Johns Hopkins, 1972. Signaling and gene transcription events in T helper lymphocytes; MHC class II protein transport.
- Michael J. McManus, Assistant Professor; M.D., Georgetown, 1983. Molecular pediatric oncology; growth factor receptors; tyrosine kinase signal transduction pathways.
- Mark A. McNiven, Associate Professor; Ph.D., Maryland, 1987. Cytoskeletal dynamics in mammalian cells; molecular basis of cellular migration during metastasis; vesicle-based transport in epithelial cells.
- L. Joseph Melton, III, Professor; M.D., LSU, 1969. Chronic disease epidemiology.
- Heidi Nelson, Associate Professor; M.D., Washington (Seattle), 1981. Colorectal cancer; immunotherapy.
- Judith R. O'Fallon, Professor; Ph.D., North Carolina, 1973. Cancer clinical trials design, conduct, and analysis.
- Dennis J. O'Kane, Assistant Professor; Ph.D., SUNY at Stony Brook, 1979. Telomerase activity as a diagnostic marker for cancer; translational research on new tumor markers.
- David H. Persing, Associate Professor; M.D./Ph.D., California, San Francisco, 1988. Precore promoter mutations in hepatic tumors; immunogenetic determinants of chronic papillomavirus infections and cervical cancer; association of chronic infections with lymphoproliferation.
- Mark R. Pittelkow, Professor; M.D., Mayo, 1979. EGF-related growth factor/receptor function: epidermal keratinocyte and melanocyte regulation of growth and differentiation.
- Karl C. Podratz, Professor; M.D./Ph.D., St. Louis, 1974. Molecular prognostic determinants in gynecologic malignancies.
- Gregory A. Poland, Professor; M.D., Southern Illinois. Expertise in vaccine development and evaluation, adjuvant development and evaluation; vaccine antigen processing and HLA presentation; and vaccine immunogenetics.
- Franklyn G. Prendergast, Professor; M.B.B.S., West Indies, 1968; Ph.D., Minnesota, 1977. Fluorescence spectroscopy; protein structure and dynamics; biochemistry and bioluminescence.
- Corey Raffel, Associate Professor; M.D./Ph.D., California, San Diego, 1980. Pediatric neuro-oncology; gene therapy and cancer.
- Jeffrey L. Salisbury, Professor; Ph.D., Ohio State, 1978. Cell cycle control; centrosomes; mitotic spindle poles; breast cancer.
- David I. Smith, Professor; Ph.D., Wisconsin, 1978. Chromosomal fragile sites; molecular genetics of cancer development.
- Thomas C. Spelsberg, Professor; Ph.D., West Virginia, 1967. Steroid action on early (*c-myc*) gene transcription, steroids and TGF- β action on bone cell functions, and early gene expression.
- Emanuel E. Strehler, Associate Professor; Ph.D., ETH Zurich (Switzerland), 1981. Intracellular Ca^{2+} homeostasis and signaling; molecular mechanisms of disease.
- Stephen N. Thibodeau, Professor; Ph.D., Washington (Seattle), 1979. Cancer genetics; colon and prostate cancer.
- Donald J. Tindall, Professor; Ph.D., North Carolina, 1973. Mechanism of androgen action in prostate cancer.
- David O. Toft, Professor; Ph.D., Illinois, 1967. Mechanisms of action of steroid receptors and heat shock proteins.
- Raul Urrutia, Assistant Professor; M.D., Cordoba (Argentina), 1987. Cell differentiation.
- Richard M. Weinshilboum, Professor; M.D., Kansas, 1967. Molecular pharmacogenetics of drug metabolism - including antineoplastic agents.

Peter J. Wettstein, Professor; Ph.D., North Carolina at Chapel Hill, 1977. Role of minor histocompatibility antigens in allograft rejection.
Anthony J. Windebank, Professor; B.M. B.Ch., Oxford, 1974. Molecular mechanisms of neurotoxic cell injury; growth factors and regeneration.
Lester E. Wold, Professor; M.D., Chicago, 1977. Immunocytochemistry; bone tumors and tumor-like conditions; breast diseases.
Charles Y-F. Young, Assistant Professor; Ph.D., Brigham Young, 1984. Calpain inhibitor-induced apoptosis in human prostate adenocarcinoma cells.

*Scottsdale campus.

Appendix F

Tumor Biology I:
Introduction to Tissue and Tumor Biology (TBIO 5000)
 2:30 - 4:00 p.m. Tue. Thur. Fall Quarter 1998
[50% participation, 25% term paper, 25% lab/problem sets]

September 29	Principles of Cell and Tissue Design	Salisbury
September 30	TBJC: Fundamentals of the Cell Cycle	
October 1	Laboratory - Light and Electron Microscopy	
October 6	Stem Cells, Differentiation, and Cancer	Maihle
October 7	TBJC: Genomic Instability/Aneuploidy	
October 8	Guest Lecture - Epigenetics and Genetics	
October 13	Properties of Transformed Cells <i>in vitro</i>	Maihle
October 14	TBJC: Temin - Hayflick	
October 15	Senescence and Immortalization	
October 20	Properties of Transformed Cells <i>in vivo</i>	Maihle
October 21	TBJC: Transgenics and Knockouts	
October 22	Xenografts	
October 27	Tissue Biology - Epithelia	Salisbury
October 28	TBJC: Cell Polarity	
October 29	Laboratory - Epithelia	
	[TERM PAPER OUTLINE DUE by 4:00 p.m.]	
November 3	Tissue Biology - Connective Tissue	Salisbury
November 4	TBJC: Invasion and Metastasis	
November 5	Laboratory - Connective Tissue	
November 10	Endothelial Cells, Vascular Tissue and Lymphatics	Salisbury
November 11	TBJC: Angiogenesis	
November 12	Laboratory - Vascular Tissue	
November 17	Pathobiology of Cancer	Salisbury
November 18	TBJC: Epithelial / Mesenchymal Interactions	
November 19	Surgical Pathology Tours	
November 24	INDEPENDENT STUDY	
November 25	INDEPENDENT STUDY	
November 26	Thanksgiving	
December 1	Normal Breast / Breast Cancer	Salisbury
	[TERM PAPER DUE by 4:00 p.m.]	
December 2	TBJC: Breast Tumor Staging and Grade	
December 3	Laboratory - Breast Pathology	
December 8	Normal Intestine / Colon Cancer	TBA
December 9	TBJC: HNPCC - MIN Mice	
December 10	Laboratory - GI Tumors	
December 17	[TERM PAPER EVALUATIONS DUE by 4:00 p.m.]	

Tumor Biology II:
Origins of Human Cancer (TBio 8000)
 2:30 - 4:00 p.m. Tue. Thur. Winter Quarter 1998
 [50% participation/50% term paper]

January 7	Origins of Human Cancer: An Overview	Mailhe
January 8	Tumor Biology Journal Club:	
January 9	Problem Set (Mailhe)	
January 14	Origins of Human Cancer: Etiology and Genetics	Smith
January 15	Tumor Biology Journal Club:	
January 16	Problem Set	
January 21	Origins of Human Cancer: Progression and Metastasis	Gendler
January 22	Tumor Biology and Journal Club: Angiogenesis	
January 23	Problem Set (Gendler and Mailhe)	
January 28	Origins of Human Cancer: Epidemiology and Prevention	Yang
January 29	Tumor Biology Journal Club: Intestinal Polyposis and COX-2	
January 30	Tumor Immunology: An Overview	Mitchell
February 4	Problem Set (Epidemiology and Prevention)	
February 5	Tumor Biology Journal Club (Tumor Immunology)	Jelinek
February 6	Problem Set (Tumor Immunology)	
February 11	Paraneoplastic Syndromes (in Breast and Ovarian Cancer)	Lennon
February 12	Tumor Biology Journal Club: Paraneoplastic Autoimmunity	
February 13	Problem Set	
February 25	Introduction to Clinical Research	O'Fallon
February 26	Tumor Biology Journal Club: Phase I Trial of Dolastatin-10	
February 27	Problem Set	
March 4	Introduction to Chemotherapy	Ames
March 5	Tumor Biology Journal Club: Inhibitors of Farnesyl Transferase	
March 6	Problem Set	
March 11	Tumor Imaging: An Overview	Robb
March 12	Experimental Tumor Imaging	Ehman
March 13	Problem Set (Mailhe)	
March 18	Introduction to Surgical Oncology	Nelson
March 19	Tumor Biology Journal Club: Surgical Procedures in Colon Cancer	
March 25	Introduction to Radiation Therapy	Bonner
March 26	Breast Cancer Patient Vignettes	
March 27	Experimental Gene Therapy	Raffel

Tumor Biology III
Growth Factors, Oncogenes, and Tumor Suppressors (TBIO 8005)
 2:30 - 4:00 p.m. Tue. Thur. Winter Quarter 1998
 [50% participation/50% term paper]

April 7	Cell Cycle and Cell Growth Control	Salisbury
April 8	Tumor Biology Journal Club	
April 9	Regulation of Immediate Early Gene Expression (AACR Meeting 3/28 - 4/1)	Getz
April 14	Growth Factors/GF Receptors	Maihle
April 15	Tumor Biology Journal Club	
April 16	Student Discussion Problem Set	
April 21	Intracellular Mediators: Kinases and Phosphatases	Maihle
April 22	Tumor Biology Journal Club	
April 23	Student Discussion Problem Set	
April 28	Intracellular Mediators: G Proteins	Karnitz
April 29	Tumor Biology Journal Club	
April 30	Student Discussion Problem Set	
May 5	Oncogenes and Viral Oncogenes	Maihle
May 6	Tumor Biology Journal Club	
May 8	Student Discussion Problem Set	
May 12 -14	INDEPENDENT STUDY	
May 19	Introduction to Tumor Suppressors	James
May 20	Tumor Biology Journal Club	
May 21	Student Discussion Problem Set	
May 26	Cancer Genetics	Jenkins/Lloyd
May 27	Tumor Biology Journal Club	
May 28	Student Discussion Problem Set	
June 2	P53 - Guardian of the Genome	James
June 3	Tumor Biology Journal Club	
June 4	Student Problem Set	
June 9	Retinoblastoma and Rb	Smith
June 10	Tumor Biology Journal Club	
June 11	Student Discussion Problem Set	
June 16	To Die Or Not To Die - Apoptosis	TBA
June 17	Tumor Biology Journal Club	
June 18	Student Discussion Problem Set	

Biology of Breast Cancer

(TBiol 5200)
Guggenheim 1093
1:30-2:30 p.m. Fridays

(50% participation/50% final exam)

- This course is aimed at integrating basic concepts in developmental, cellular and molecular biology of the breast together with current information on the etiology, diagnosis and treatment of breast cancer.
- The faculty include members from diverse basic science and medical disciplines including cell and molecular biology, pathology, oncology and surgery.

April 11	Breast Cancer: The Magnitude of the Problem	Ingle
April 18	Development, Anatomy and Histology and Cell Biology of the Breast	Salisbury
April 25	Histopathology of the Breast	Wold
May 2	Experimental Models of Breast Cancer	Gendler
May 9	Oncogenes, Growth Factors, and Breast Cancer	Leof
May 16	Tumor Suppressors and Breast Cancer	Mr. Ritland
May 23	Radiation Therapy for Breast Cancer	Peterson
May 30	Surgical Treatment of Breast Cancer	Donohue
June 6	Breast Cancer Diagnosis and Imaging	Johnson
June 13	Systemic Therapy for Breast Cancer	Ingle
June 20	Experimental Therapies for Breast Cancer	Maihle
June 27	Final Examinations Due (by 5:30 p.m.)	

Principles in Pancreatic Cancer

(TBiol 5200)
Guggenheim 1093
3:00-4:00 p.m. Fridays

- This course is aimed at integrating basic concepts in developmental, cellular and molecular biology of the pancreas together with current information on the etiology, diagnosis and treatment of pancreatic cancer.
- The faculty include members from diverse basic science and medical disciplines including cell and molecular biology, pathology, clinical gastroenterology, oncology and surgery.

- October 25 Pancreatic Cancer: What is the Problem?
 Dr. Eugene P. DiMagno, Gastroenterology Research Unit, SMH
- November 1 Development, Cell Biology and Histology of the Pancreas
 Dr. Raul Urrutia, Gastroenterology Research Unit, SMH
- November 8 Histopathology of Pancreatic Cancer
 Dr. Lawrence J. Burgart, Surgical Pathology
- November 15 Experimental Models of Pancreatic Cancer
 Dr. Raul Urrutia, Gastroenterology Research Unit, SMH
- November 22 Cellular and Molecular Mechanisms of Pancreatic Cancer
 Dr. Raul Urrutia, Gastroenterology Research Unit, SMH
- December 6 Current and Future Non-Surgical Treatments of Pancreatic Cancer
 Dr. Richard M. Goldberg, Medical Oncology
- December 13 Surgical Treatment of Pancreatic Cancer
 Dr. Michael Sarr, Gastroenterology Research Unit and Surgery, SMH

For more information contact
Dr. Raul Urrutia (4-7500)

Business of Science, Science of Business

TBio 5300

K. E. Bennet, M.B.A. and N. J. Maihle, Ph.D.

Summer Quarter (even years)

- 1) Introduction (August 2) Orientation and Objectives [KEB/NJM]
- 2) Administrative Structures in Support of Research (August 5) [KEB]
Not-for-Profit & For Profit
- 3) Overview of Research Accounting (August 7) [KEB]
Research Budgets
Direct versus Indirect costs
- 4) Sources of Financial Support for Research (August 9) [NJM]
Intramural & Extramural Support
Federal & Private
- 5) Sources of Financial Support for Research (August 12) [KEB]
Corporate
Strategic Alliance, Joint Development
Licensing/Venture Capital
- 6) Introduction to Intellectual Property (August 14) [KEB]
Definition of Intellectual Property
Protection of Intellectual Property
Patents & Trade Secrets
Ownership of Intellectual Property
- 7) Introduction of Cases (August 16) [KEB]
- 8) Commercialization of Research Discoveries (August 21) [KEB]
Licensing
Market Value of Invention
- 9) Independent Study on Cases (August 19)
- 10) Laws and Policies Governing Conduct of Research (August 23)
Institutional [NJM]
State, Federal, and International [KEB]
- 11) Case Presentations "Levamisole" (August 26) [KEB/NJM]
- 12) Case Presentations - "University of Florida" (August 28) [KEB/NJM]
- 13) Course Wrap-Up (August 30) [KEB/NJM]

Origins of Human Cancer: Normal Breast & Breast Cancer

1/13/98 TBIO II 8000

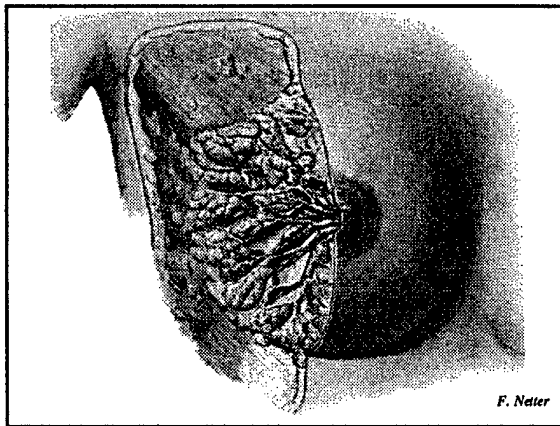
Tumor Biology II (8000)
Origins of Human Cancer

Normal Breast Development and Histology, and Breast Cancer

January 13, 1998
Jeffrey L. Salisbury, Ph.D.

Normal Breast

- compound, branched, alveolar gland
 - 15-25 irregular lobes
- terminal duct lobular unit (lobules: functional secretory unit in lactation)
 - ducts: lactiferous ducts, lactiferous sinus (ampulla), extralobular ducts, lobular ducts, alveolar ducts (terminal ductules)
 - alveoli
 - lining epithelium
 - surrounding myoepithelial cell layer (oxytocin responsive)
- adipose and connective tissue

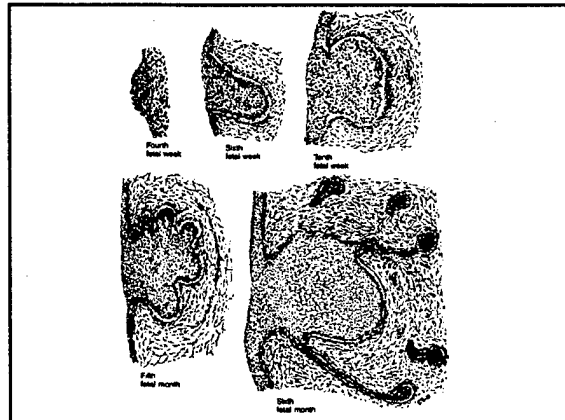


Mammary Gland Development

- four developmental stages
 - embryonic
 - adolescent
 - lactating
 - involution

Embryonic Stage

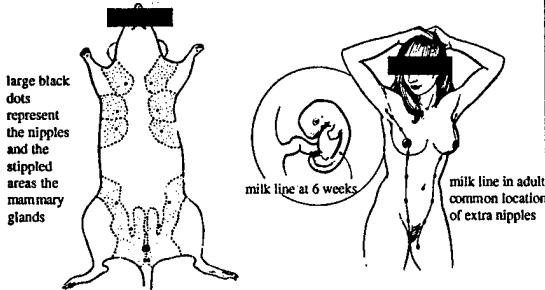
- 'primitive milk streak' (human week 5 embryo)
 - thickened epithelial layer derived from ectoderm
- mammary ridge or milk line (mouse day 11, human week 6-7)
 - raised epidermal tissue 4-6 cell layers both sides of ventral midline, other portions involute
- mammary bud (disc, globular, cone ⇒ bud)
 - centers of cellular migration and shape changes (mouse 5-6 per side, humans only 1 per side)
- 15-25 secondary buds ⇒ mammary cord (human 5th fetal month)
 - rapid proliferation ⇒ cord opens at skin (nipple)
 - proliferation at opposite end ⇒ branching ducts
- development ceases until puberty



Origins of Human Cancer: Normal Breast & Breast Cancer

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Mammary System of the Mouse and Milk Line in Human Fetus and Corresponding Location in Adult



Breast Development in the Male

- identical to female until day 13-15 gestation
- mesenchyme condenses around center of mammary bud, and cells of the cord die
 - small segment of the cord detaches from superficial epidermis ⇒ mammary rudiment (no further development)
- + testosterone ⇒ cell death, bud degeneration
- - testosterone ⇒ male mammary development

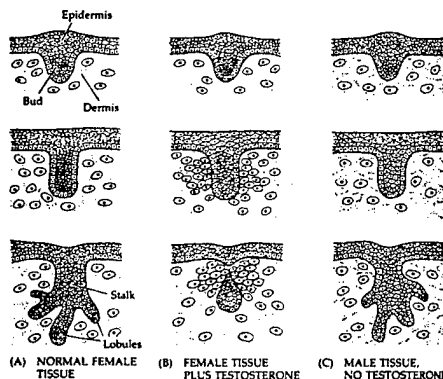
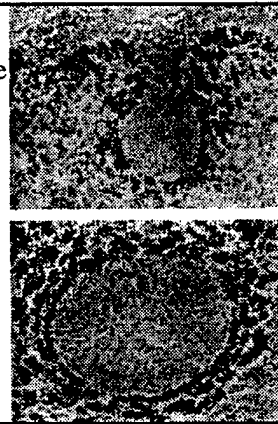
Mammary rudiment in male mouse fetus. The rudiment has separated from the epidermis.



^3H -Dihydrotestosterone Receptor Radioautography

(A) Median section through a mammary rudiment, epidermis at top. Steroid-binding mesenchymal cells are found only around the gland bud and its stalk.

(B) Oblique section through an epithelial gland bud. There is a well defined envelope of receptor-positive mesenchymal cells around the epithelium, indicating the short range of inductive influence.



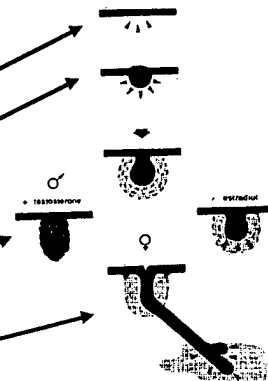
Epithelial-Mesenchyme Interactions in the Mouse.

mesenchyme induces epithelial mammary ridge to proliferate

young bud induces fibroblastic 'mammary' mesenchyme (w/androgen & estrogen receptors)

day 14 male, testosterone ⇒ mesenchyme to destroy epithelial anlage

day 16-17 female, 1st sprout invades fat pad, further growth and branching



Origins of Human Cancer: Normal Breast & Breast Cancer

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Hormonal Regulation of Growth & Function

- puberty
 - estrogen (ovary) \Rightarrow growth of duct system
 - progesterone (ovary) \Rightarrow alveoli development
- pregnancy
 - estrogen (ovary & placenta) \Rightarrow growth of duct system
 - progesterone (ovary & placenta) \Rightarrow alveoli development
 - prolactin (pars disalis of hypophysis) \Rightarrow full glandular devel.
- birth
 - estrogen \downarrow , progesterone \downarrow , prolactin \uparrow \Rightarrow lactation
- regression
 - nursing \emptyset , prolactin \downarrow \rightarrow lactation \downarrow , epithelium degenerates, connective tissue \uparrow

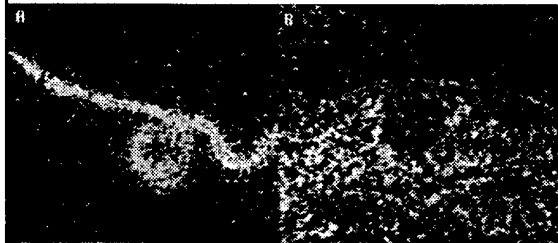
Role of Growth Factors

- TGF β family
 - generally inhibitory for breast epithelial growth
 - TGF β 1 inhibits ductal growth by \emptyset DNA S in end buds (not in stromal cells or proliferation of lobuloalveolar structures)
 - TGF β 2 & 3 \Rightarrow disappearance of proliferating mammary stem cell layer, involution of ductal end buds, & cessation of glandular growth
 - TGF β \downarrow synthesis and secretion of milk proteins and limit their accumulation during pregnancy
 - TGF β over expression in transgenic mice
 - \Rightarrow general mammary hypoplasia
 - \Rightarrow reduced mammary ductal branching
 - \Rightarrow failure of lobuloalveolar development

Role of Growth Factors

- TGF α and EGF (autocrine & paracrine)
 - mitogens for normal and malignant epithelial cells
 - over expression in transgenic mice
 - \Rightarrow mammary hyperplasia
 - \Rightarrow increased incidence of carcinoma
 - \Rightarrow shorter latency following chemical carcinogenesis
- KGF keratinocyte growth factor (FGF family)
 - secreted by stromal cells
 - \Rightarrow stimulate epithelial cell proliferation
 - \Rightarrow ductal & acinar cell growth

in situ hybridization for KGFR and KGF in mammary rudiments



14 day female mouse embryos.



Whole mount of cleared mouse mammary fat pad week 4 to 6 illustrating terminal endbuds. Hematoxylin stain.

Nipple and Areola

- accessory areolar glands of Montgomery
 - intermediate between sweat glands and true mammary glands
- sebaceous glands (usually lacking hair follicles)
- sweat glands
- smooth muscle (inner, intermediate, outer layers)
- connective tissue (circular, elliptic course)
- richly innervated (Meissner's corpuscles, Merkel's discs, Krause's end bulbs, Pacinian corpuscles)

Origins of Human Cancer: Normal Breast & Breast Cancer

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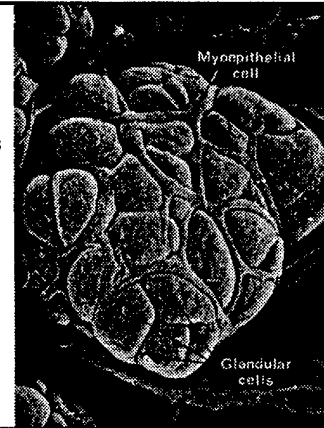
Inactive Breast

- **parenchyma** (sparse and consists mainly of duct elements)
 - cuboidal epithelial cells and myoepithelial cells
- **stroma** (abundant)
 - loose irregular cellular connective tissue immediately surrounding ducts
 - dense irregular connective tissue beyond the area of the lobule
 - fat

SEM of an Acinus of the Mammary Gland

Branching myoepithelial cells occupy the grooves between the bases of the secretory cells.

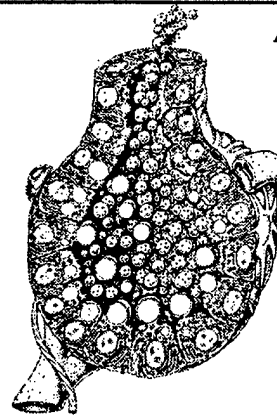
(from: Nagao, T. Cell Tissue Res 209:1, 1980)



Lactating Mammary Gland

- **parenchyma** (abundant and consists mainly of alveolar elements)
 - cuboidal epithelial cells
 - myoepithelial cells
 - product within lumen of alveoli and ducts
- **stroma** (reduced)
 - small amount of connective tissue between alveoli and septa between lobules
- lymphocytes often present

Acinus of a Lactating Mammary Gland

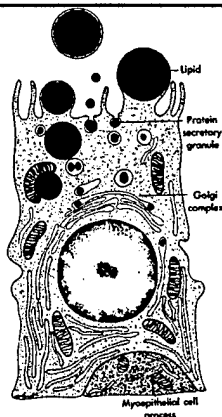


Identify:

- A) lipid droplets
- B) casein granules
- C) secretory cells
- D) myoepithelial cells
- E) capillary

Secretion in Breast Alveolar Cells

- **merocrine** (exocytotic)
 - milk proteins casein, lactalbumin
- **apocrine**
 - (loss of portion of cell membrane and some cytoplasm)
 - lipid droplets
- **diffusion**
 - water, ions
- **transcytosis**
 - IgA



Breast Cancer

- **Incidence:**
 - 180,000 new cases per year
 - 1:8 women in US and Canada (lifetime risk)
 - rare before age 20, rarely diagnosed in < age 25
 - past age 25 incidence rises steadily to peak around menopause
- **Deaths**
 - 45,000 deaths annually (US)
 - second most common cause of cancer death

Origins of Human Cancer: Normal Breast & Breast Cancer

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Risk Factors

- High (relative risk > 4.0)
 - age
 - personal history BC
 - family history
 - proliferative disease w/atypia
 - Moderate (relative risk 2-4)
 - first degree relative w/ BC
 - personal history ovarian, or endometrial cancer
 - age 1st full term pregnancy >30
 - nulliparous
 - obesity, postmenopausal
 - upper socioeconomic class
 - Low (relative risk > 1-2)
 - menarche before age 12
 - menopause after age 55
 - Caucasian race
 - moderate alcohol intake
 - long duration estrogen replacement therapy (>15 years)
- * ACS estimates that 75% breast cancer occurs in women with no known high-risk factors

Invasive Carcinomas of Breast Cancer

Histological Type	Frequency	5-year survival
Infiltrating ductal carcinoma	63.6 %	79
Infiltrating lobular carcinoma	5.9	84
Infiltrating ductal & lobular	1.6	85
Medullary carcinoma	2.8	82
Mucinous (colloid) carcinoma	2.1	95
Comedocarcinoma	1.4	87
Paget's Disease	1.0	79
Papillary Carcinoma	0.8	96
Tubular carcinoma	0.6	96
Adenocarcinoma, NOS	7.5	65
Carcinoma, NOS	3.5	62

Noninvasive Carcinomas of Breast Cancer

Histological Type	Frequency	5-year survival
Intraductal carcinoma (DCIS)	3.6 %	> 99
Lobular carcinoma <i>in situ</i> (LCIS)	1.6	> 99
Intraductal & LCIS	0.2	> 99
Papillary carcinoma	0.4	> 99
Comedocarcinoma	0.3	> 99

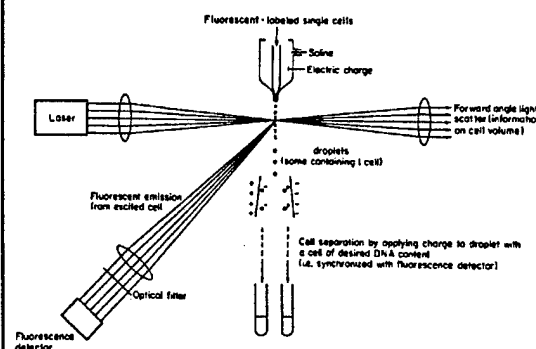
Hormone Receptor Status

- cancers which display estrogen receptors have a better prognosis (ER+)
 - differentiated
 - respond to hormonal manipulation
 - tamoxifen (anti-estrogen) treatment ~75% ER+ patients respond
- significance of progesterone receptor (PR) status less well understood
 - generally ER+ are also PR+
 - cancers that are PR+ and ER- have a worse prognosis

Additional Markers

- Cathepsin D (acidic lysosomal protease)
 - correlation with metastasis
- C-erb B-2 (C-neu)
 - correlation with high nuclear grade and aneuploidy

Flow Cytometry

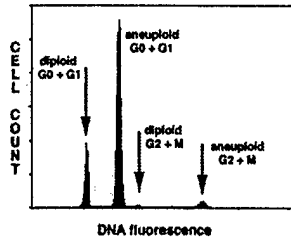


Origins of Human Cancer: Normal Breast & Breast Cancer

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Flow Cytometry

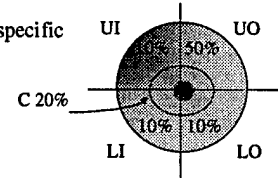
- diploid normal cell population
- aneuploid tumor cells in general have a poorer prognosis
- Flow Cytometry is a rapid method for determining the degree of aneuploidy in a tumor sample



Aneuploidy and low S phase

Diagnostic Procedures

- self-examination
 - regular basis to follow normal breast architecture
 - 1 cm tumor (detectable) 5-10 years
- mammography
 - most sensitive and specific
- location of cancers



(Histology) Grading (modified Scarff-Bloom-Richardson)

Tubule Formation (% carcinoma composed of tubular structures)	Score
> 75	1
10-75%	2
less than 10%	3
Nuclear Pleomorphism	Score
small, uniform shape and staining	1
moderate increase in size and variation	2
marked variation	3
Mitotic Count (per 10 high power fields)	Score
up to 7	1
7 to 14	2
15 or more	3

Grade calculated by adding the scores. Grade correlates with survival.

Grade	Score	5-year survival (%)	7-year survival (%)
1	3 to 5	95	90
2	6 or 7	75	65
3	8 or 9	50	45

Stage in Breast Cancer is Based on Size and Degree of Spread.

Stage	Definition	Survival (%)	
		5-year	7-year
I	Tumor ≤ 2 cm, N0, M0	96	72
II	Tumor >2<5 cm, N1,M0 or >5, N0,M0	81	71
III	Tumor any size,N2, M0	52	39
IV	Tumor any size, N0-3, M1	18	11

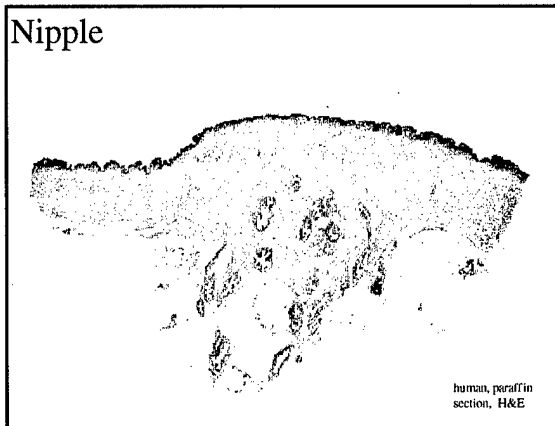
Treatment

- Primary or Local-Regional Therapy
 - Breast Conservation Surgery (lumpectomy + axillary dissection + XRT)
- Systemic Therapy
 - Hormonal Therapy
 - Tamoxifen (nonsteroidal anti-estrogen and estrogen-like activity)
 - Megace (progestational agent)
 - Halotestin (an androgen)
- Chemotherapy
 - adriamycin (A), cyclophosphamide (C), methotrexate (M), 5-fluorouracil (F), vincristine/vinblastin, mitomycin, dsplatin
 - most common combination CMF, CAF, or AC

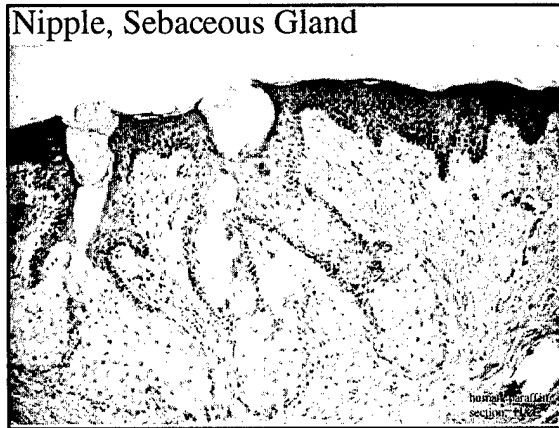
Origins of Human Cancer: Normal Breast & Breast Cancer

1/13/98 TBIO II 8000

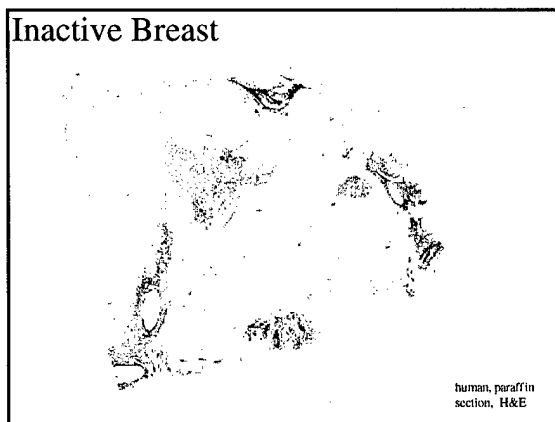
Nipple



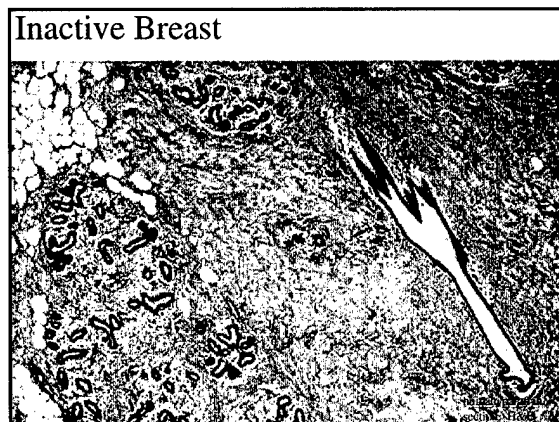
Nipple, Sebaceous Gland



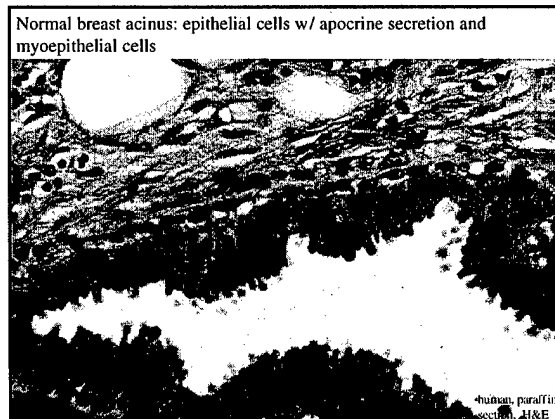
Inactive Breast



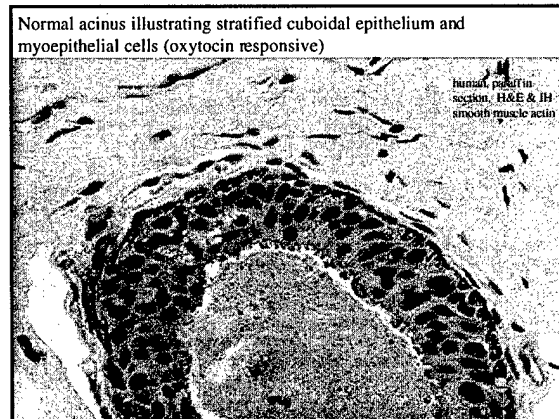
Inactive Breast



Normal breast acinus: epithelial cells w/ apocrine secretion and myoepithelial cells

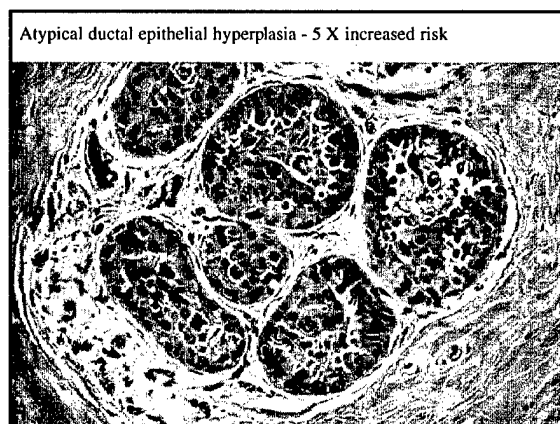
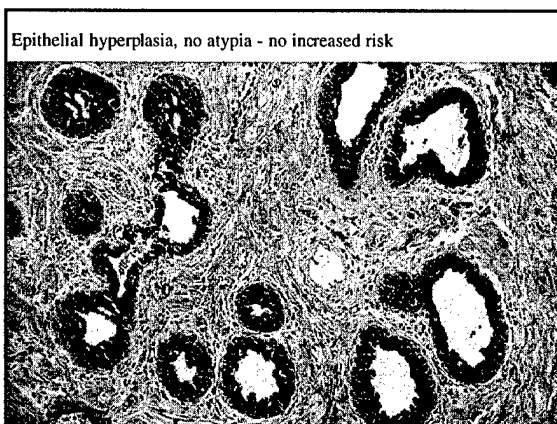
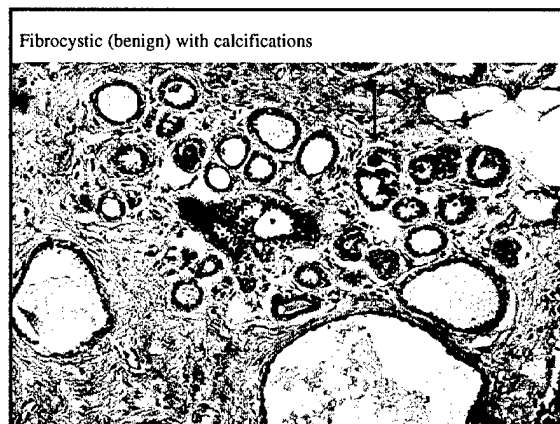
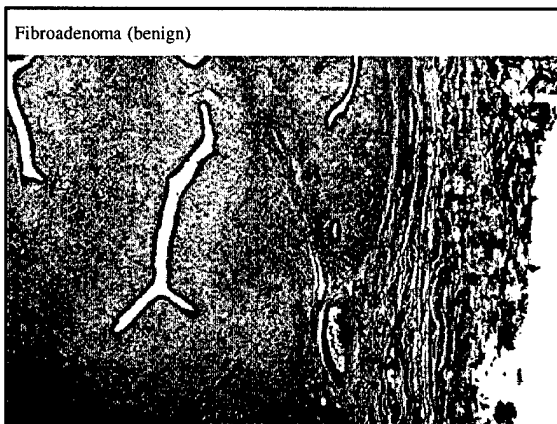
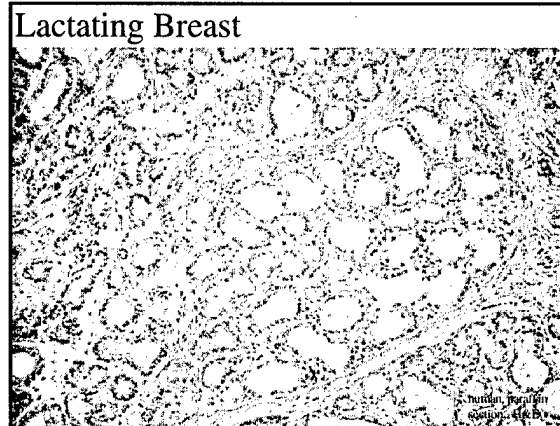
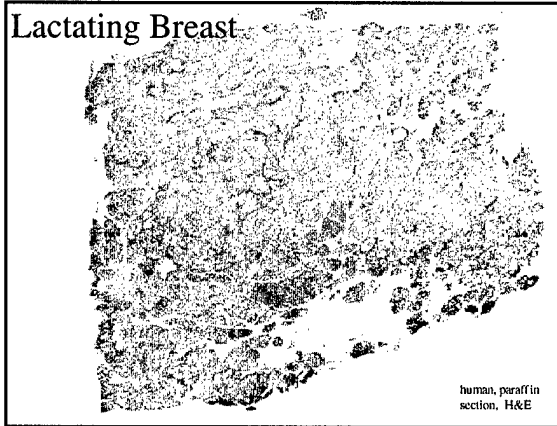


Normal acinus illustrating stratified cuboidal epithelium and myoepithelial cells (oxytocin responsive)



Origins of Human Cancer: Normal Breast & Breast Cancer

1/13/98 TBIO II 8000



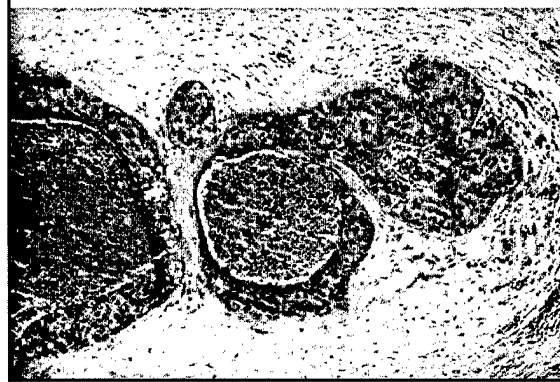
Origins of Human Cancer: Normal Breast & Breast Cancer

1/13/98 TBIO II 8000

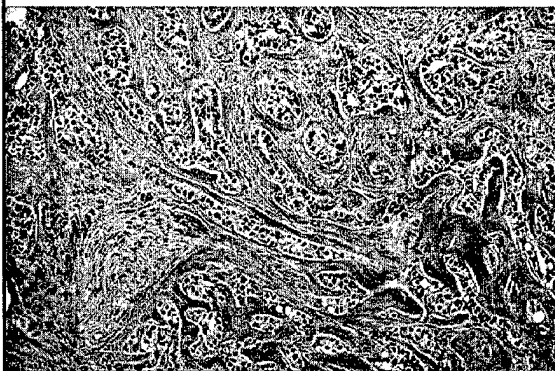
Intraductal carcinoma (DCIS)



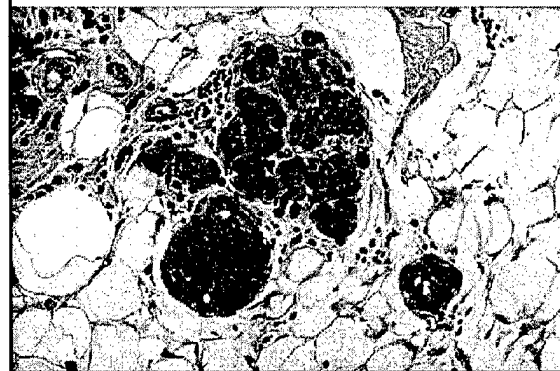
Comedocarcinoma pattern of intraductal carcinoma



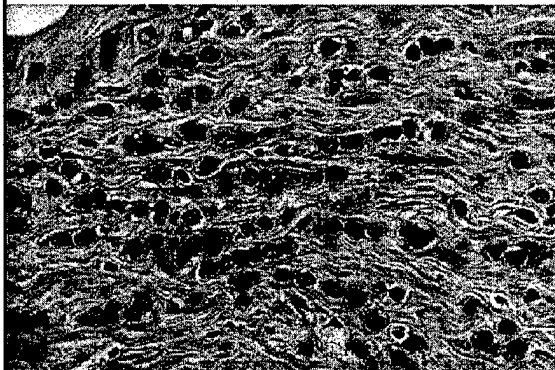
Infiltrating ductal carcinoma



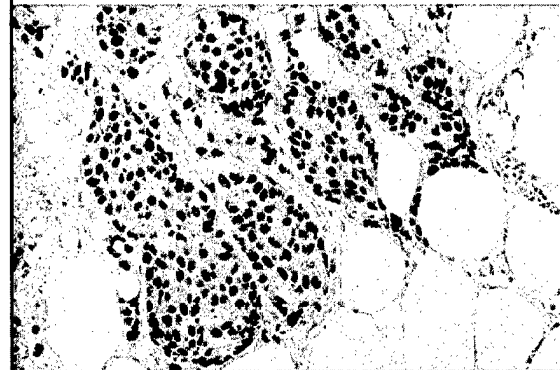
Lobular carcinoma *in situ*



Invasive lobular carcinoma



Estrogen receptor positive breast carcinoma



Appendix G

Current Topics in Tumor Biolog.

(TBiol 5151)

2:30 - 3:30 p.m. Wednesdays

Journal Club Topics and (Presenter) Academic Year 1997-1998

- 10/1 Expression genetics in cancer: Shifting the focus from DNA to RNA. Ruth Sager (1997) *Proc. Natl. Acad. Sci. USA* 94: 952-955.
Expression of maspin in prostate cells is regulated by a positive Ets element and a negative hormonal responsive element site recognized by androgen receptor. Ming Zhang, David Magit, and Ruth Sager (1997) *Proc. Natl. Acad. Sci. USA* 94: 5673-5678 (Ms. **Julie Johnson**)
- 10/8 Normal genetically mosaic mice produced from malignant teratocarcinoma cells. Beatrice Mintz and Karl Illmensee (1975). *Proc. Natl. Acad. Sci. USA* 72: 3585-3589.
Successive generations of mice produced from an established culture line of euploid teratocarcinoma cells. Timothy Stewart and Beatrice Mintz (1981) *Proc. Natl. Acad. Sci. USA* 78: 6314-6318 (Mr. **Michael Rogers**)
- 10/15 The Werner syndrome protein is a DNA helicase. Gray, Shen, Kamath-Loeb, Blank, Sopher, Martin, Oshima, and Loeb, (1997). *Nature Genetics* 17:100-103.
(Ms. **Nohelia Canales**)
- 10/22 Differences between the ribonucleic acids of transforming and nontransforming avian tumor viruses. P.H. Duesberg and P.K. Vogt (1970) *Proc. Natl. Acad. Sci. USA* 67:1673-1680.
DNA related to the transforming gene(s) of avian sarcoma viruses is present in normal avian DNA. D. Stehelin, H.E. Varmus, J.M. Bishop, P.K. Vogt (1976) *Nature* 260:170-173.
Transformation of chicken cells by the gene encoding the catalytic subunit of PI3-kinase. Chang, et al., (1997, *Science* 276:1848-1850)
(Mr. **Eric Calhoun**)
- 10/28 Life and Cancer Without Telomerase. V.A. Zakian (1997) *Cell* 91:1-3.
Telomere shortening and tumor formation by mouse cells lacking telomerase RNA. M.A. Blasco et al., (1997) *Cell* 91:25-34. (Ms. **Colleen Schehl**)
- 11/12 Embryonic lethality and radiation hypersensitivity mediated by Rad51 in mice lacking Brca2. Sharan et al., (1997) *Nature* 386:804-810.
Targeted mutations of breast cancer susceptibility gene homologs in mice: lethal phenotypes of Brca1, Brca2, Brca1/Brca2, Brca1/p53, and Brca2/p53 nullizygous embryos. Ludwig et al., (1997) *Genes and Development* 11:1226-1241.
Brca2 is required for embryonic cellular proliferation in the mouse. Suzuki et al., (1997) *Genes and Development* 11:1242-1252.
(Dr. **Cecelia Boardman**)
- 11/19 Regulation of gene expression by small molecules. Gottesfeld et al., (1997) *Nature* 387:202-205.
Discrimination of 5'-GGGG-3', 5'-GCGC-3', and 5'-GGCC-3' sequences in the minor groove of DNA by eight-ring hairpin polyamines. Swalley et al., (1997) *J. Amer. Chem. Soc.* 119:6953-6961.

Recognition of seven base pair sequences in the minor groove of DNA by ten-ring pyrrole-imidazole polyamide hairpins. Turner et al., (1997) *J. Amer. Chem. Soc.* 119:7636-7644.
(Ms. Gwen Lomberg)

- 1/14 The role of histological grading in the prognosis of patients with carcinoma of the breast. N.E. Roberti, (1997). *Cancer* 80:1708-1716.
Histological grade as a prognostic factor in breast carcinoma. H. Burke and D.E. Henson, (1997) *Cancer* 80:1703-1705.
Consensus conference on the classification of ductal carcinoma *in situ*. G. Schwartz et al., (1997) *Cancer* 80:1798-1802.

(Ms. Colleen Schehl)

- 1/21 Suppression of glioblastoma angiogenicity and tumorigenicity by inhibition of endogenous expression of vascular endothelial growth factor. S-Y. Cheng et al, (1996). *Proc. Natl. Acad. Sci.* 93:8502-8507.
Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1 mutant. B. Millauer et al., (1994). *Nature* 367:576-578.

(Ms. Julie Johnson)

- 1/28 Localization of Kaposi's sarcoma-associated herpesvirus in bone marrow biopsy samples from patients with multiple myeloma. J.W. Said, et al., (1997). *Blood* 90:4278-4282.
Kaposi's sarcoma-associated herpesvirus infection of bone marrow dendritic cells from multiple myeloma patients. M.B. Rettig et al., (1997). *Science* 276:1851-1854.
Kaposi's sarcoma-associated herpesvirus infection and multiple myeloma. C. Parravicini et al., (1997). *Science* 278: 1969-1973.
HHV-8 and multiple myeloma in France, and the UK. A-G Marcelin et al., and MacKenzie et al., (1997). *The Lancet* 350:603-604.

(Mr. Andy Danielsen)

- 2/4 Recent Advances in Chemoprevention of Cancer. W.K. Hong and M.B. Sporn, (1997). *Science* 278:1073-1077.
Tamoxifen Breast Cancer Prevention Trial - An Update. L.G. Ford and K.A. Johnson (1997). *in: Etiology of Breast and Gynecological Cancers*. Wiley-Liss Inc. pages 271-282.

(Mr. Kun Xu)

- 2/25 Natural History of Cervicovaginal Papillomavirus Infection in Young Women. G.Y.F. Ho et al., (1998). *New Engl. J. Med.* 338:423-428.
HPV Infection in Women Infected with the Human Immunodeficiency Virus. X.W. Sun et al., (1997). *New Engl. J. Med.* 337:1343-1349.
HPV and Anogenital Cancer. K.V. Shah (1997). *New Engl. J. Med.* 337:1386-1388.
Genetic Alterations Accumulate during Cervical Tumorigenesis and Indicate a Common Origin for Multifocal Lesions. A.A. Larson et al., (1997). *Cancer Research* 57:4171-4175.

(Ms. Gwen Lomberg)

- 3/4 Regulated expression of the diphtheria toxin A chain by a tumor-specific chimeric transcription factor results in selective toxicity for alveolar rhabdomyosarcoma cells. E.S. Massuda et al., (1997). *Proc. Natl. Acad. Sci. USA.* 94:14701-14706.
Chromosomal translocations in human cancer. T.H. Rabbitts (1994). *Nature* 372:143-149.

(Mr. Eric Calhoun)

- 3/11 The Yin and Yang of T Cell Costimulation. J.P. Allison and M.F. Krummel, (1995). *Science* 270:932-933.
Enhancement of Antitumor Immunity by CTLA-4 blockade. D.R. Leach, M.F. Krummel, AND J.P. Allison, (1996). *Science* 271:1734-1736.
(Mr. Jonathan Hoyne)
- 3/18 Conservation of the Chk1 Checkpoint Pathway in Mammals: Linkage of DNA Damage to Cdk Regulation Through Cdc25. Y. Sanchez et al., (1997). *Science* 277:1497-1501.
Mitotic and G2 Checkpoint Control: Regulation of 14-3-3 Protein Binding by Phosphorylation of Cdc25C on Serine-216. C.-Y. Peng et al., (1997). *Science* 277:1501-1505.
(Mr. Kurt Krummel)
- 3/25 p53-Dependent Apoptosis Modulates the Cytotoxicity of Anticancer Drugs. S.W. Lowe, E.H. Ruley, T. Jacks, and D. Housman, (1993). *Cell* 74:957-967.
Uncoupling of S Phase and Mitosis Induced by Anticancer Agents in Cells Lacking p21. T. Waldman, C. Lengauer, K. Kinzler, and B. Vogelstein, (1996). *Nature* 381:713-716.
(Ms. April Blajeski)
- 4/8 Splicing into Senescence: The Curious Case of p16 and p19^{ARF}. Daniel A. Haber (1997). *Cell* 91:555-558.
Tumor Suppression at the Mouse INK4a Locus Mediated by the Alternative Reading Frame Product p19^{ARF}. T. Kamijo, et. al., (1997). *Cell* 91:649-659.
(Dr. Jill Reiter)
- 4/15 Trans receptor inhibition of human glioblastoma cells by erbB family ectodomains. D.M. O'Rourke et al., (1997). *Proc. Natl. Acad. Sci.* 94:3250-3255.
The enhanced tumorigenic activity of a mutant epidermal growth factor receptor common in human cancers is mediated by threshold levels of constitutive tyrosine phosphorylation and unattenuated signaling. H-J. Su Huang et al., (1997). *J. Biol. Chem.* 272:2927-2935.
(Mr. Jonathan Hoyne)
- 4/22 Matrix adhesion and Ras transformation both activate a phosphoinositide 3-OH kinase and protein kinase B/Akt cellular survival pathway. A. Khwaja et al., (1997). *EMBO*. 16:2783-2793.
(Mr. Kun Xu)
- 4/29 A serine/threonine kinase gene defective in Peutz-Jeghers syndrome. A. Hemminki et al., (1998). *Nature* 391:194-186.
Cloning and characterization of a novel serine/threonine protein kinase expressed in early *Xenopus* embryos. J-Y Su et al., (1996). *J. Biol. Chem* 271:14430-14437.
(Ms. Susan Barrett)
- 5/6 Forced degradation of Fas inhibits apoptosis in adenovirus-infected cells. A.E. Tollefson et al., (1998). *Nature* 392:726-730.
(Dr. Cecelia Boardman)
- 5/20 Serial Analysis of Gene Expression. V. Velculescu, L. Zhang, B. Vogelstein, and K. Kinzler (1995). *Science* 270:484-487.
Gene Expression Profiles in Normal and Cancer Cells. L. Zhang, W. Zhou, V. Velculescu, S. Kern, R. Hruban, S. Hamilton, B. Vogelstein, and K. Kinzler (1995). *Science* 276:1268-1272.
(Mr. Eric Calhoun)



Maihle, N.J.

Appendix H

Mayo Education

► Graduate School

[Intro](#)
[Programs](#)
[Faculty](#)
[M.D.-Ph.D. Program](#)
[Patient-Oriented Research](#)
[Undergrad Research](#)
[Facilities](#)
[Support & Housing](#)
[How to Apply](#)
[Mayo's Communities](#)

Medical School

Graduate School of Medicine

School of Health-Related Sciences

School of CME

International Education

Alumni Association

Medical Libraries

Faculty Research Interests

Advanced courses, tutorials, seminars and journal clubs provide the depth of knowledge you will require to become an expert in your chosen field of study. Because our student-to-faculty ratio is low, classes frequently use small-group, interactive tutorial settings.

Listed below are brief descriptions of each of the areas of specialization offered by Mayo Graduate School.

Biochemistry and Molecular Biology

This program has 23 primary appointees and 29 faculty (representing 16 different departments and divisions) with secondary appointments. Students can choose from a diverse array of research opportunities including the regulation of gene expression and cell growth, steroid hormone action, DNA replication, oncogenesis, human molecular genetics and molecular biophysics.

The faculty contact person is:

Frank M. Rusnak, Ph.D.
 Department of Biochemistry and Molecular Biology
 507-284-2289
rusnak@mayo.edu

Biomedical Imaging

This program's 25-member faculty and their laboratories offer training in the methods of biomedical imaging science and clinical imaging investigations. Particularly strong components include computer visualization, confocal microscopy, computed tomography (including dynamic), magnetic resonance imaging (including functional), ultrasound imaging and virtual reality.

The faculty contact person is:

Richard A. Robb, Ph.D.
 Department of Physiology and Biophysics
 507-284-2997
rar@mayo.edu

Immunology

A faculty of 17 investigators provides students with access to this rapidly growing field. Research opportunities include allergy, cellular immunology, immunogenetics, immunopharmacology, molecular biology, molecular immunology, immunochemistry, neuroimmunology, tumor immunology, autoimmunity, immunoparasitology and rheumatology.

The faculty contact person is:

Larry R. Pease, Ph.D.
 Department of Immunology
 507-284-9891
pease@mayo.edu

Molecular Neuroscience

This inter-departmental program has a 35-member faculty and 30 independent laboratories that focus on the neurobiological processes related to human disease. Strengths include molecular biology, membrane and channel biophysics, signal transduction, receptor pharmacology, neural networks, three-dimensional imaging and neural cell biology.

The faculty contact person is:

Anthony J. Windebank, M.D.
Molecular Neuroscience Program
507-284-8729
windebank.anthony@mayo.edu

Pharmacology

A faculty of 16 scientists and research laboratories associated with this program focus on the biochemical and physiological processes that underlie the action of drugs. Current areas of investigation include intracellular transduction mechanisms, pharmacogenetics, molecular neuropharmacology, cancer chemotherapy, receptor biology, cardiovascular pharmacology, muscle contraction, immunopharmacology, pharmacokinetics, mass spectrometry, drug metabolism and membrane function.

The faculty contact person is:

Cynthia T. McMurray, Ph.D.
Department of Pharmacology
507-284-2747
mcmurray@mayo.edu

Physiology and Biophysics

A 22-member faculty leads a variety of investigative projects in cellular and systemic physiology. The program emphasizes the study of ion channels, fast microscopic imaging of cells, smooth muscle physiology, gastrointestinal physiology, cardiovascular and pulmonary physiology, renal physiology and hypertension.

The faculty contact person is:

Richard A. Robb, Ph.D.
Department of Physiology and Biophysics
507-284-2997
rar@mayo.edu

The Biology of Breast Cancer and Tumor Biology

This integrated, multi-disciplinary program offers specialized training in the biology of cancer, especially women's cancers. The 32-member faculty have research and clinical appointments in a broad range of medical and research specialties. The program's research strengths include gene regulation, cell cycle control, oncogene and tumor suppressor action, tumor immunology, signal transduction, anti-tumor pharmacology, and the biology of breast, ovarian, uterine, lung, gastrointestinal and prostate cancers.

Supported in part by a grant from the USAMRMC Breast Cancer Research Program: DAMD 17-94-J-4116.

The faculty contact person is:

Jeffrey L. Salisbury, Ph.D.
Department of Biochemistry and Molecular Biology
507-284-4070
salisbury@mayo.edu

[Next...M.D.-Ph.D. Program]

Medical School Assistant Professor in Cell Biology

The Department of Cell Biology and Neuroanatomy seeks applications for a tenure track assistant professor position. All areas of cell biology will be considered, but particular consideration will be given to research directed at signal transduction mechanisms. Candidates will be expected to develop a strong, independent research program that leads to external funding. Applicants must possess a Ph.D. or equivalent degree and have at least two years of postdoctoral experience. Candidates must be U.S. citizens or be able to secure permanent resident status and must provide verification of highest degree. Strong candidates will have significant publications in high quality peer-reviewed journals and will be engaged in research that complements the departmental strengths in cell biology, developmental biology and neuroscience. A demonstrated ability to interact and collaborate will be favored. The teaching assignment will be in appropriate departmental courses that are offered to professional students, undergraduates, or graduate students in several interdepartmental programs. Candidates should send curriculum vitae, statement of research interests, and arrange for three reference letters to be sent to: Hasina Hason, University of Minnesota, Department of Cell Biology and Neuroanatomy, 4-144 Jackson Hall, 321 Church St. S.E., Minneapolis MN 55455. The last date for receipt of applications is March 1, 1998.

The University of Minnesota is an equal opportunity educator and employer.

(NW4834)A



Tumor Biology Program Mayo Graduate School

Graduate Training in Tumor Biology: The Mayo Graduate School Tumor Biology Program is a multidisciplinary predoctoral training program in the biology of cancer. Research and training in this program is broadly focused on gene regulation, cell cycle control, cancer genetics, oncogene and tumor suppressor action, tumor immunology, signal transduction, antitumor pharmacology, and the biology of breast, ovarian, uterine, lung, G.I., brain, and prostate cancers. Students participate in laboratory-based research, as well as a formal tumor biology curriculum that integrates current concepts in cell growth control with the natural history of human tumors. The Tumor Biology Program is supported in part by a training grant from the USAMRMC Breast Cancer Research Program. DAMD 17-94-J-4116. The Mayo Clinic is located in Rochester, Minnesota, a city with approximately 75,000 population. Mayo Clinic is an equal opportunity employer. Women and minorities are encouraged to apply. Inquiries and application materials can be obtained from the Mayo Graduate School by email at: phd@mayo.edu

(NW4846)A

Cato Research Ltd. (CRL),

is a contract research organization with locations in Research Triangle Park, NC, Washington, DC, and Montreal, Canada. CRL engages in the planning and execution of regulatory strategy for pharmaceutical and biological product development. Our goal is to assist clients in developing and gaining regulatory approval for products in conventional and cutting-edge therapeutic areas and novel drug delivery technologies.

Our company has exciting non-laboratory opportunities at all corporate locations for self-starters with scientific backgrounds who want to learn and grow in a creative environment. These positions require excellent written and verbal communication skills, strong initiative and interpersonal abilities, and sound critical and analytical thinking. All positions require an M.D. or Ph.D. with expertise in toxicology, pharmacokinetics, infectious disease, immunology, oncology, pharmacology or other biological sciences.

Clinical Research Scientists

We are seeking individuals with clinical and scientific training to provide leadership in ensuring that client contracts are met. These opportunities require the ability to design, direct, coordinate and manage drug development and regulatory activities. The ideal candidates will have 5-8 years of experience in the pharmaceutical or biotech industry and knowledge of the entire drug development process.

Clinical Research Fellows

The Fellows receive training in the scientific, regulatory, medical and financial aspects of pharmaceutical drug development. The ideal candidates will possess a Ph.D. in Biological Sciences and the ability to manage multiple tasks.

If you are an excellent communicator and a team player with problem-solving skills, and wish to expand your career, you will find these opportunities challenging and professionally rewarding.

Cato Research Ltd. offers complete salary and benefits packages. For application to all CRL offices, please send your resume, cover letter and writing sample to: **Job 400, Cato Research Ltd., 200 Westpark Corp. Ctr., 4364 S. Alston Ave., Durham, NC 27713-2280.** No phone calls, please. EOE

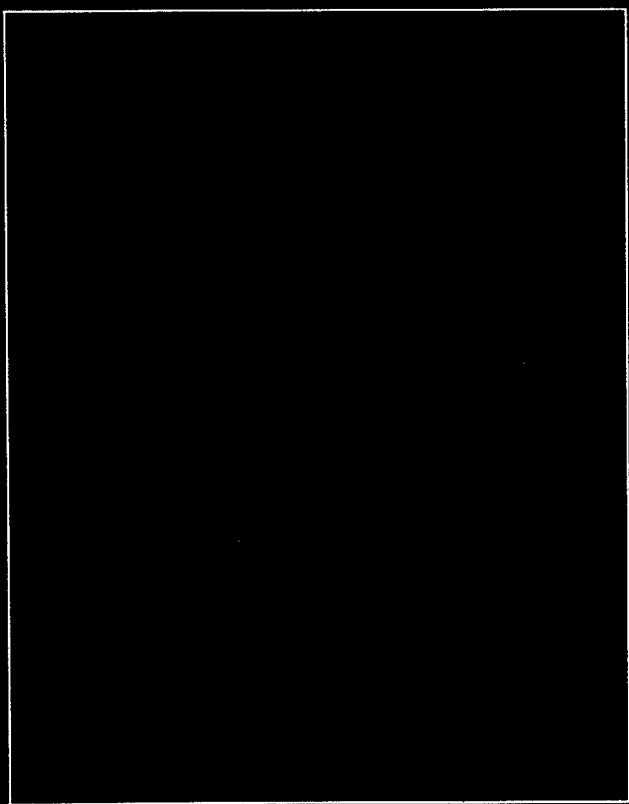
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Maihle, N.J.

Appendix J



M A Y O

Ph.D. Degree

Students in the Tumor Biology Track must complete the following, in addition to the 13 core credit requirement.

TBio	5000	Tumor Biology I: Introduction to Tumor Biology	3 cr.
TBio	5100	Research Seminars in Tumor Biology	1 cr.
TBio	5150	Current Topics in Tumor Biology	1 cr.
TBio	5300	The Business of Science and the Science of Business	1 cr.
TBio	5858	Laboratory Rotations in Tumor Biology (2 cr./rotation - 3 rotations req.)	6 cr.
TBio	8000	Tumor Biology II: Origins of Human Cancer	2 cr.
TBio	8005	Tumor Biology III: Growth Factors, Oncogenes, and Tumor Suppressors	3 cr.
TBio	8200	Cell Biology of Cancer	3 cr.

In addition, all students in the Tumor Biology Program shall register for the Animal Care and Use Training Sessions and the American Association of Cancer Research (AACR) course in Histopathology of Cancer. Additional advanced elective courses in any area may be taken to fulfill the overall degree requirements of 42 credits.

The Tumor Biology program is supported in part by a predoctoral training award from the USAMRDC entitled "Biology of Breast Cancer."

TUMOR BIOLOGY

- TBio 5000f. *TUMOR BIOLOGY I: INTRODUCTION TO TUMOR BIOLOGY*. (3 cr) Maihle, Tindall
Material to be covered includes fundamental concepts and methods in tumor biology, as well as normal tissue histology and tumor pathobiology.
- TBio 5100f,w,s,su. *RESEARCH SEMINARS IN TUMOR BIOLOGY*. (1 cr/yr) Maihle, Salisbury
Informal presentation of intramural research findings from the laboratories involved in relevant research investigations. Discussions will be based on chalk-talk format with the open research notebook. In addition, speakers from outside the institution will present throughout the year. All Tumor Biology trainees will be expected to present their research plans/findings in this forum annually and will be encouraged to actively participate in this highly multidisciplinary exchange of ideas and information.
- TBio 5150f, w,s. *CURRENT TOPICS IN TUMOR BIOLOGY*. (1 cr) Salisbury, Maihle
This journal club will discuss current primary literature covering all aspects of tumor biology with an emphasis on women's cancers. The journal club will meet once per week and be conducted under the open discussion format with directed student and faculty presentations. During the fall quarter, journal articles of fundamental and historic interest in the area of tumor biology will be read and discussed. Topics to be covered include: cell cycle, oncogenes, tumor suppressors, growth factors, signal transduction, metastasis, DNA tumor viruses, retroviruses.
- TBio 5200f. *PRINCIPLES OF PANCREATIC CANCER*. (1 cr) Urrutia
Anatomy, fine structure, and embryology of the pancreas. Basic cell biology and regulation of pancreatic gene expression. Cellular and animal models for the study of normal and neoplastic pancreatic cell differentiation. Epidemiology, etiology, diagnosis and management of pancreatic cancer.
- TBio 5250w. *GENE THERAPY AND CANCER*. (1 cr; odd yrs) Federspiel, Salisbury
Current papers in the area of gene therapy and cancer will be reviewed and discussed in the journal club format. Students in the Tumor Biology program will participate in all sessions and will present a paper during the quarters that they are enrolled in this journal club.
- TBio 5300su. *THE BUSINESS OF SCIENCE AND THE SCIENCE OF BUSINESS*. (1 cr; offered even years) Bennet, Maihle
This course reviews concepts fundamental to the commercial potential of biotechnology. Topics include current patent issues in biotechnology, regulatory issues in biotechnology and research funding mechanisms, as well as the grant review process.

TBio 5858f,w,s,su. *LABORATORY ROTATIONS IN TUMOR BIOLOGY* (2 cr)
Staff
Tutorial course involving general techniques, instrumental analysis, and special procedures undertaken in the laboratory of choice. In addition, the student will assimilate the general research area of the laboratory through readings, lab meetings, and discussion. Students and faculty shall use these rotations to determine the degree of general mutual interest in research topics for potential thesis projects.

TBio 8000w. *TUMOR BIOLOGY II: ORIGINS OF HUMAN CANCER*. (3 cr; prereq TBio 5000) Maihle, Tindall
Topics to be covered include: basic tumor biology, oncogenes, tumor viruses, anti-oncogenes (tumor suppressors), tumor immunity, cancer chemotherapy, and biological response modifiers. Also listed under Molecular Biology 8250.

TBio 8005s. *TUMOR BIOLOGY III: GROWTH FACTORS, ONCOGENES, AND TUMOR SUPPRESSORS*. (3 cr; prereq TBio 5000, TBio 8000) Maihle, Tindall
This course will focus on the mechanisms by which growth factors and oncogenes influence cell growth and division. Topics include: transmembrane signal transduction; cell cycle and regulation of cell division; ontogeny of oncogenes; mechanisms of oncogene activation; the insulin receptor family; PDGF/sis and PDGF receptor; EGF receptor/c-erb B 1 and 2 (neu); introduction to hematopoietic growth factors/receptors; receptors which lack intrinsic kinase activity, ras family of oncogenes; introduction to nuclear signal transduction; chromosome/DNA-binding proteins; development and differentiation; wound-healing and angiogenesis; carcinogenesis in humans; and anti-oncogenes. Also listed under Molecular Biology 8370.

TBio 8200w. *CELL BIOLOGY OF CANCER*. (2 cr; offered even years; prereq TBio 5000) Salisbury, Gendler, Lingle
This course will cover normal histology and the histopathology of neoplasia and will consist of one lecture and one laboratory session each week. Normal development and microscopic anatomy of the four basic tissue types will be covered, followed by a detailed examination of integument, hemopoietic system, male and female reproductive tracks, respiratory system, and GI track. Specific primary and metastatic tumors of each system will also be covered. The laboratory session will involve study of microscopic slide preparations and problem set discussion sessions.

TBio 8305s. *BIOLOGY OF BREAST CANCER*. (1 cr; offered odd years) Maihle, Salisbury
This course will cover the cell and developmental biology of the breast and the histopathobiology of breast tumors. Experimental models for breast cancer, growth factors, oncogenes, and tumor suppressers in breast cancer will be covered. Clinical topics including radiation and chemotherapy, surgical treatments, diagnosis, and experimental therapies in breast cancer will also be presented.

TBio 8400 *MASTER'S PROJECT IN TUMOR BIOLOGY* (3 cr) Staff
Readings and/or research in Tumor Biology culminating in the submission of the Master's Project. Topics will be chosen by the student in consultation with the adviser and the student's advisory committee.

Research

TBio 8840f,w,s,su. *RESEARCH IN TUMOR BIOLOGY*. Staff
Graduate thesis research for Master's students under supervision of staff.

TBio 8900f,w,s,su. *RESEARCH IN TUMOR BIOLOGY*. Staff
Graduate thesis research under supervision of staff.

Biology of Breast Cancer Program Extramural Training Support

<u>Grant #</u>	<u>P.I.</u>	<u>Source</u>	<u>Term</u>	<u>Total Direct</u>
T32 CA 75926	Salisbury, J.L.	NCI	7/1/98-6/30/03	\$805,414
	Biology of Cancer: A Predoctoral Training Program			
DAMD J-4116-3	Maihle, N.J.	US Army	9/1/94-8/31/98	\$370,154
	Biology of Breast Cancer: A Predoctoral Training Program			
NRSA	Baines, J.E.	NIH	9/15/97-5/31/02	
	Novel Immunotherapeutic Approaches to Cervical Cancer			
NRSA	Canales, N.D.	NIH	5/1/97-5/1/02	
	Research Training in Breast and Ovarian Cancer			



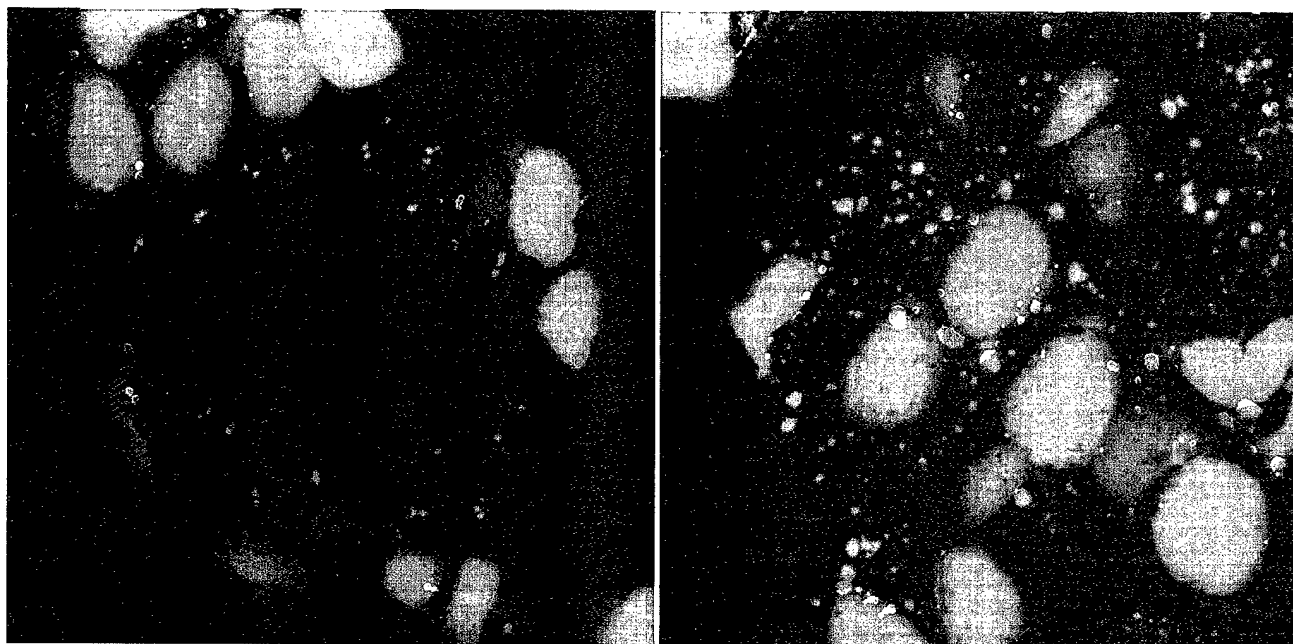
Mayo Graduate School

Self Study for External Review

1998

Biology of Breast Cancer:

A Predoctoral Training Program



Fluorescence images of nuclei (red) and centrosomes (green) in normal human breast tissue (left) and a human breast tumor (right). From W. Lingle, W. Lutz, J. Ingle, N. Maihle, and J. Salisbury (1998). *Proc. Natl. Acad. Sci. USA* 95:2950-2955.

"For, if we would serve science, we must extend her limits, not only as far as our own knowledge is concerned, but in the estimation of others."

Rudolf Virchow, 1859

Biology of Breast Cancer:

**A multidisciplinary predoctoral training program in the
biology of breast cancer.**

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Biology of Breast Cancer:

A Program for Graduate Training in Tumor Biology

The goals of the Biology of Breast Cancer and Tumor Biology Training Program are four-fold:

- First, to provide trainees with a solid and uniquely multidisciplinary knowledge base in the biology of cancer using breast cancer as the paradigm.
- Second, to guide the development of each individual trainee so that they achieve their fullest academic and research potential.
- Third, to aid trainees in the establishment of their professional network of peers and colleagues in the field of breast cancer research.
- Fourth, to stimulate new working alliances between students, fellows, and staff participating in breast cancer research, education, and clinical endeavors at the Mayo Clinic and within the Mayo Cancer Center.

Overview

The "Biology of Breast Cancer" is a multidisciplinary predoctoral training program in the biology of cancer, with a specific emphasis on breast cancer. The focus of the program is to provide an educational environment that stimulates excellence in scientific thought and training while simultaneously providing exposure to all of the major fields of study relevant to tumor biology. While a defining feature of this program is its research focus and integral link with clinical aspects of breast cancer, a general foundation in tumor biology is both important and essential in achieving this goal. The curriculum for this program is outlined in the course syllabus material, provided below, and the thesis research topics of the students matriculating in the program. This information clearly details and substantiates the major breast cancer research focus of this new training program. Research and training are broadly focused on gene regulation, cell cycle control, cancer genetics, oncogene and tumor suppressor action, tumor immunology, signal transduction, antitumor pharmacology, with a particular emphasis on breast cancer, but also includes investigators with research programs in ovarian, uterine, lung, G.I., brain, and prostate cancers. Students participate in laboratory-based research, as well as in a formal tumor biology curriculum that integrates current concepts in cell growth control with the natural history of human tumors.

The Biology of Breast Cancer Training Program has been supported by extramural training grants since its inception. Currently, these training grants include an award from the US Army Medical Research and Materiel Command in the "Biology of Breast Cancer" (DAMD17-94-J-4116), and a T32 Training Grant from the National Cancer Institute in "Tumor Biology" (CA75926). In addition, the program operates under the generous support of the Mayo Foundation through the Mayo Graduate School and the Mayo Cancer Center. Individual trainees also have been successful in competition for individual research awards.

Program Structure

Administrative Structure

The training program is administrated through the Mayo Graduate School, and is closely allied with the Mayo Cancer Center. Day-to-day program administration operates largely through the Director (Dr. Salisbury) and Co-director (Dr. Maihle) of the Biology of Breast Cancer and Tumor Biology Training grants. Long range planning and administration operates through the Tumor Biology Education Committee (Drs. Salisbury, Maihle, Federspiel, Jelinek, and Tindall, and a trainee, Mr. J. Baines). The Education Committee meets each academic quarter to discuss student recruitment, student progress, and coordination within the Tumor Training Program curriculum. In addition, the directors of the three cancer-related pre- and postdoctoral training grants (Drs. Salisbury, Maihle, Getz, and David) and the Director of the Mayo Cancer Center (Dr. Prendergast) interact to coordinate ongoing programs and activities related to cancer research and education at Mayo in general. The Biology of Breast Cancer Training faculty also meet quarterly, in addition to frequent interactions through participation in program courses, journal clubs, research workshops, and a biweekly social hour called the "Tumor Biology Tea."

Qualifications of the Program Faculty

The training faculty consists of approximately 50 full and associate members drawn from each of the basic science departments, as well as clinical faculty who participate in scholastic activities of the program but who do not have active research laboratories. The level of individual faculty participation varies each year for specific courses, topics and journal clubs. Nonetheless, a growing and enthusiastic cadre of participating faculty has emerged. In future years the program may elect to restructure its faculty based on degree of faculty participation, given the mounting enthusiasm for this program, as well as recent and ongoing recruitment of new staff in the area of cancer biology. At this time, however, faculty privileges will remain as they are in order to promote both the inclusively and multidisciplinary nature of this new training program. A listing of the participating faculty is given on pages 23-25. While most individual faculty are associated with traditional discipline-based basic science and clinical departments (such as Oncology, Molecular Biology, Experimental Pathology, Pharmacology, etc.) the administrative structure of the Program is that of an interdisciplinary programmatic unit. This programmatic structure reflects the interdisciplinary nature of the major research and academic efforts of the associated faculty.

- Full members of the training faculty have an established track record of accomplishment in biomedical research as demonstrated by significant publications of high scientific merit, excellence, and innovation. Overall, the faculty have consistent records of extramural funding in support of their individual research programs.
- The collective interests of this training faculty are quite broad, but all show direct breast cancer relevance. These interests include: cell signaling, cancer genetics, gene regulation, tumor immunology, oncogene and tumor suppressor action, cell cycle regulation, tumor virology, gene therapy, hormonal regulation, and molecular cytology. Most training faculty are also members of the NCI-designated Mayo Cancer Center.
- Faculty drawn from both clinical and basic science departments contribute to the Training Program through participation in a variety of relevant educational activities and as clinical instructors. Faculty from outside the program may serve as advisory members of qualifying examination and thesis committees, however, they may not serve as research mentors for students in the Biology of Breast Cancer Training Program.

Program Curriculum

Introduction

The program curriculum and thesis research is a predoctoral training program leading to the Ph.D. degree in Biomedical Sciences. Each year, 3 to 5 students are accepted into the program for an appointment term of 4 to 5 years. The program strives to maintain a steady state level of 15 to 20 students. Trainee stipends initially are supported through institutional funds. Students qualify for support from extramural training grants (third through fifth year), following successful completion of the qualifying examination. The training program curriculum includes didactic course work, journal clubs, research seminars and workshops, and tutorial and special clinical activities. Students who matriculate into the program must meet the general course requirements of the Mayo Graduate School in which a minimum of 15 credits are required from the Graduate School Core Curriculum. Students must also complete 20 credits from the didactic Tumor Biology Program curriculum and the remainder of their credit requirements can be completed through elective courses offered by the Tumor Biology Program, the Mayo Graduate School or by special topics courses given at other institutions and sanctioned by the Mayo Graduate School. For students in the Biology of Breast Cancer Program these electives must include a course entitled "Biology of Breast Cancer." A student's program of core courses is individually developed by the Education Committee in consultation with the student and his/her advisor.

Summary of the Curriculum:

Graduate School Core Offerings (15 Credits, minimum)

- Genome Biology (3)
- Immunology (3)
- Principles of Cell and Tissue Design (3)
- Biochemistry (3)
- Genetics (1)
- Pharmacology (2)
- Developmental Biology & Statistics (1)
- Biology of Disease (1)
- Ethics (1)

Required Biology of Breast Cancer Course Offerings (20 Credits)

- Tumor Biology I: Introduction to Tissue and Tumor Biology (3)
- Tumor Biology II: Origins of Human Cancer (3)
- Tumor Biology III: Growth Factors, Oncogenes, and Tumor Suppressors (3)
- Biology of Breast Cancer (1)
- Current Topics in Tumor Biology: Journal Club (1) x 3
- Research Seminars in Tumor Biology and Tumor Biology Interest Group (1)
- AACR Course in Histopathology of Cancer, Keystone CO. (1)
- Laboratory Rotations in Tumor Biology (3 required rotations, 2 credits each = 6 total)
- Research in Tumor Biology (Thesis Research (0))

Recommended Electives

- Quantitative Biology I-III, Neuroscience (1), Integrated Physiology (5)
- Tumor Immunology (1), Business of Science and the Science of Business (1)
- Cytogenetics (2)

Biology of Breast Cancer Track and Core Curriculum Schedule

Year I or II Fall Quarter	M	T	W	Th	F
9:00-10:00	Biochemistry	Immunology	Biochemistry	Immunology	Biochemistry
10:00-11:00	Genome Biology		Genome Biology		Genome Biology
11:00-12:30	Tumor Biology I		Tumor Biology Journal Club		Tumor Biology I

Year 1 or II Winter Quarter	M	T	W	Th	F
9:00-10:00	Cell Biology	Genetics	Cell Biology		Cell Biology
11:00-12:30	Tumor Biology II		Tumor Biology Journal Club		Tumor Biology II

Year 1 or II Spring Quarter	M	T	W	Th	F
9:00-10:00	Pharmacology		Pharmacology		Pathobiology
10:00-11:00			Development + BioStatistics		
11:00-12:30	Tumor Biology III		Tumor Biology Journal Club		Tumor Biology III

Core Courses	Tumor Biology Courses
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Additional advanced elective courses may be chosen in any area from the Mayo Graduate School Bulletin to fulfill the overall degree requirement of 35 credits. In addition, all students in the training program are required to take formal classes in Radiation Safety, Animal Care and Use, and also participate in an NIH Grant Writing Workshop. These required courses are not administrated by the Mayo Graduate School, and, therefore, are not offered for Graduate School credit.

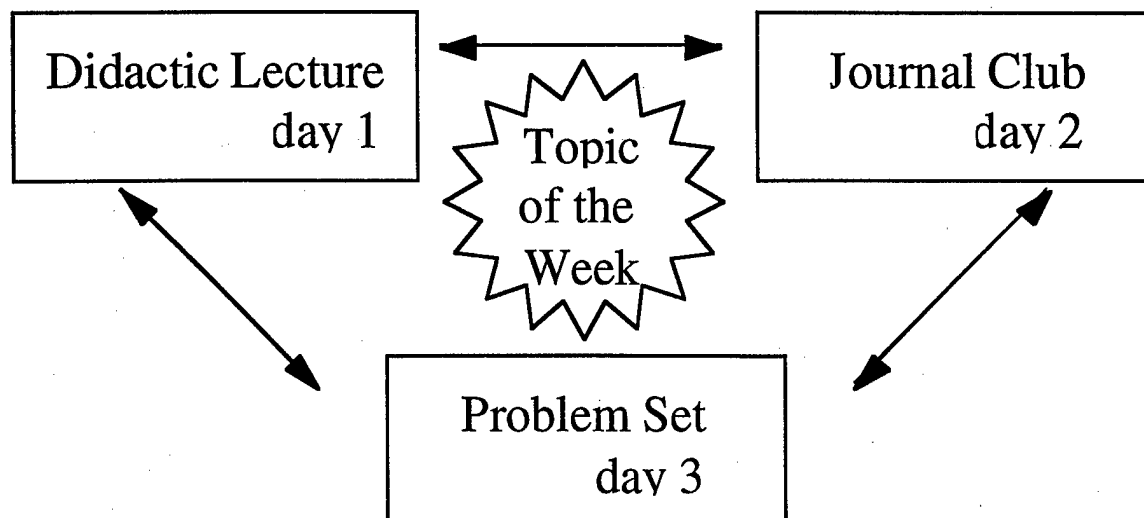
Program Implementation

Innovative Strategies for Teaching

Tumor Biology track courses establish a solid foundation in the biology of cancer. In practice, the biology of breast cancer is emphasized as an illustrative paradigm throughout the program curriculum. Issues of fundamental importance to understanding breast cancer are also relevant to other cancers, and the converse is also true. Likewise, there are many instances where the illustrating example of a relevant point may involve biological systems as diverse as yeast and frogs (not breast cancer research, but directly relevant to improving our understanding of breast cancer). Thereby, the tumor biology curriculum is grounded in basic cancer biology with the aim of leading students to a thorough understanding of all aspects at the forefront of breast cancer research. In order to accomplish this, our curriculum has been strategically developed to provide a strong foundation in the study of cancer using breast cancer as the model wherever possible. For example, to illustrate the significant emphasis on and integration of breast cancer in the overall curriculum, topics in breast cancer are featured in three 3 credit hour courses in the curriculum (see below), as well as in approximately one out of every three journal club presentations. Moreover, *all* trainees are required to register for a didactic course in "The Biology of Breast Cancer" (TBIO 8305, page 134 in the Mayo Graduate School Bulletin). The three major courses were organized and are taught using breast cancer as the principle paradigm for instruction and content: "Introduction to Tissue and Tumor Biology" (Tumor Biology I, TBIO 5000), "Origins of Human Cancer" (Tumor Biology II, TBIO 8000), and "Growth Factors, Oncogenes and Tumor Suppressors" (Tumor Biology III, TBIO 8005).

Tumor Biology Track courses share several distinguishing features and innovative strategies for teaching which enhance learning and student/faculty participation.

- **Course Structure:** Tumor Biology I, II, and III are given as an integrated series during the first three consecutive quarters following matriculation. Individually, these courses meet three times per week (1 1/2 hour per session) with an overview and historical review of a selected topic(s) for the current week presented in a didactic lecture format during the first class session. This is followed by a student presentation of a current or historically relevant research paper(s) in the area of the week's topic during the second class session using the journal club format. Finally, a round table small group problem set discussion format is used to focus on questions and problems relevant to the week's topic during the third class session. The research paper presentation and problem set discussions are carefully organized in order to thoroughly integrate research topics relevant to the theme of the week. The effectiveness of these active learning/teaching strategies is apparent to all participants in these courses. The active involvement of students in the learning and discovery process, in information processing, and in the application of information to problems requires that students are accountable for learned information on an immediate and ongoing basis. Problem centered learning also puts learning into context and facilitates learning transfer. These sessions allow students to organize and categorize information into meaningful units and to 'discover' novel relationships and extract and assimilate important points in an interactive and participatory manner.



- **Balance of Historic and Current Scientific Perspectives:** Given the rapid pace of progress in the biological sciences and the exponential rate of growth of relevant literature the general philosophy that is promoted within the program is to *teach less better*. The objective here is to lay a strong foundation in cancer biology with the clear understanding that what is particularly relevant and important today, may not be so tomorrow. Therefore, emphasis is placed on developing effective learning skills, and the application of these skills to both historic paradigms, as well as critical review and evaluation of issues at the forefront of modern cancer biology.
- **Commitment, Accountability, and Responsibility:** Integral to the Tumor Biology Program teaching philosophy is *Peer Performance Assessment* and the *Team Learning Model*. These strategies create a climate in which all students are encouraged to grow. This results in a classroom environment where students from diverse backgrounds (including clinical fellows) feel welcome to fully participate in discussions and problem solving. In this way, desired student performances are tied directly to the efforts of the students themselves, to the involvement of students in the teaching-learning process, to the opportunities to make choices, and to the degree to which they interact with their peers and instructors. Emphasis is placed on organization and presentation skills, accountability tracking, and peer assessment and feedback. Our experience with this learning model is that trainees rapidly gain a level of professional expectation of their peers (and themselves) that both promotes and enhances the general level of academic and scholastic effort among trainees.
- **Continuing Education:** Senior students who have completed the formal didactic course requirements, and postdoctoral fellows who are supported by other cancer-related training grants actively participate in the journal club sessions that are an integral component of the Tumor Biology curriculum. In this way, senior trainees contribute to the critical mass of the class and also enhance the sophistication and the multidisciplinary nature of the discussions. Through this mechanism, more advanced trainees revisit current topics in cancer biology throughout their advanced training years. In this manner, advanced trainees have the opportunity to reinforce key concepts, to help new trainees better understand these concepts, and also to remain current with the rapid pace of development in the dynamic field of cancer biology. Likewise, Program faculty (and their laboratory personnel) actively participate in these regular weekly journal club sessions.
- **Integration of the Clinical Perspective:** The training program is designed to give the trainee a broad and well-rounded understanding of cancer from the basic science,

population science, and clinical perspectives. Integration of the clinical activities of the Mayo Cancer Center into the training program is achieved in several ways:

- ◇ First, clinical fellows and residents from a broad spectrum of cancer relevant programs (e.g., oncology, hem/onc, orthopedic research, gynecologic oncology, pediatric oncology, etc.) formally enroll and participate in training program courses and journal clubs. Active participation by clinical residents and fellows adds considerably to the multidisciplinary perspective of the student body, and to stimulating class discussions.
- ◇ Second, clinical staff give didactic lectures in areas of their specialty in Biology of Breast Cancer Training Program courses. For example in Tumor Biology II and III, individual lectures are given by clinical staff practicing in Surgery, Medical Oncology, Radiation Oncology, and Surgical Pathology.
- ◇ Third, program trainees are required to attend Mayo Cancer Center Research Workshops, Mayo Cancer Center Grand Rounds, and appropriate departmental, Research Society, Oncology Society and Hematology Society lectures, and receive course credit for participating in these activities (TBio 5101: "Research Seminars in Tumor Biology"). Students are made aware of relevant speakers through Email, direct mailings, and weekly announcements during the weekly journal club.
- ◇ The program curriculum is integrated with clinical practice wherever possible through special course related activities. For example, small group tours of the Surgical Pathology Suite (in TBio I) allow students to observe gross dissection of surgical specimens (including breast tumors), rapid freezing and cryomicrotomy, microscopic examination (via video monitors) and diagnosis by staff pathologists, and reporting to operating room surgeons. Additionally, Tumor Biology Program trainees are required to attend clinical rounds with a Mayo staff member (any division or department). Direct exposure to clinical activities such as these are useful for students to understand, based on first-hand observation, the intensity, dedication, and skill involved in the clinical care and treatment of cancer patients. These activities also promote the involvement of our clinical faculty in Biology of Breast Cancer Training Program activities.
- ◇ Finally, Tumor Biology trainees may have one or more clinical staff advisors participate as members of their Thesis Advisory Committee. Sometimes this involvement is fairly technical, e.g., participation by a Mayo Cancer Center biostatistician in study design and analysis. In other instances, however, clinical advisors may be directly involved in helping the trainee define a clinically relevant question, and/or assist them with tumor specimen acquisition and/or data analysis.

Additional Academic Activities

Seminars by Students, Faculty and Invited Speakers: Extensive institutional resources support seminars by nationally and internationally recognized scientists and clinicians on the Mayo Rochester campus. Approximately 350-400 speakers come to the Rochester campus each year. Trainees are, therefore, exposed to diverse biomedical research opportunities, and institutionally and departmentally-based research seminars throughout the year. In December of 1997, students of the Tumor Biology Program hosted Dr. Judah Folkman (Harvard University) who presented the Annual Findling Lecture of the Mayo Graduate School. The 1998-1999 academic year will feature a series of visiting speakers who will focus on the broad topic of Epigenetics and Cancer. During each of their research years, Tumor Biology Trainees also present research seminars and research posters in multidisciplinary research workshops and retreats (e.g., the Mayo Graduate School Annual Research Symposium, the Joint Mayo Cancer Center/Laboratory Medicine Retreat). More recently, we have formalized the Tumor Biology Interest Group (TBIG) for Mayo Graduate

School course credit. This monthly research workshop provides the opportunity for all Tumor Biology trainees (pre- and postdoctoral) to regularly present their research plans, proposals, and results in a constructively critical internal forum.

Attendance at National Research Meetings: All students are supported to attend at least one national scientific meeting each year even if they are not presenting an abstract. If they are presenting their work, attendance at additional meetings is encouraged and supported by the research mentor's laboratory. Mentors take an active role in introducing students to the professional culture and 'networking' critical to success in any biomedical research career through this mechanism. In recent years, Biology of Breast Cancer Training Program trainees have attended and presented at the following national meetings: AACR, ASCB, FASEB, Annual Oncogene Meetings, Annual Human Cancer Meeting, Cold Spring Harbor Cancer Genetics Meetings, Salk Tyrosine Phosphorylation Meetings, and various Gordon and Keystone Conferences.

Research Training

Selection of Thesis Laboratory, Mentor, and Thesis Committee Members: Trainees typically matriculate in June through August and are required to complete three laboratory-based (minimum 8 weeks each) rotations during their first year. Any laboratory-based Mayo Graduate School faculty member may serve as a mentor for these research rotations. Selection of the thesis mentor follows completion of successful laboratory-based rotations by mutual consent of the student and mentor with the sanction of the Training Program Education Committee and Mayo Graduate School Education Committee. The qualifying examination consists of a written thesis proposal, an oral presentation (TBIG forum), and its defense before a thesis committee consisting of a minimum of 4 faculty (including the thesis advisor), and when appropriate, an extramural committee member from outside the institution. Typically clinical or extramural committee members' research specialties are related to the general area of the student's thesis topic. Following successful completion of the qualifying examination, research progress is assessed through regular Thesis Advisory Committee meetings (minimum of one Thesis Advisory Committee meeting per year). While Thesis Advisory Committee members are available for advice, technical assistance, and consultation throughout the year, these meetings provide a formal opportunity for input by the Thesis Advisory Committee on progress and experimental aspects of the thesis project. The chair of the Thesis Advisory Committee formally reports the outcome of each committee meeting in writing to the Training Program Education Committee and to the Mayo Graduate School.

Thesis Research: The Biology of Breast Cancer Training Program places strong emphasis on thesis research. All laboratory-based faculty have demonstrated records of research training at both the predoctoral and postdoctoral levels. The specific details of an individual student's research training plan are developed following the selection of a thesis advisor and in consultation with the Thesis Advisory Committee. The thesis research project must be *hypothesis driven and experimental in nature* and must, in addition, have a *direct relevance to the biology of cancer*.

Ph.D. Thesis: The thesis is the most important document that the Ph.D. candidate prepares during the course of graduate study, and is a record of the scientific accomplishments that justify the awarding of the Ph.D. degree. The thesis is archival. Consequently, the Mayo Graduate School has developed standards for its format and style, and our trainees adhere to these guidelines. The thesis examination consists of a formal thesis research seminar open to all members of the Mayo community followed by a meeting with the Thesis Examining Committee during which the scientific merit and accomplishments of the candidate are evaluated. Successful completion of a research thesis typically also results in two or more research manuscripts submitted for publication in peer-reviewed journals of high scientific standards.

Student Recruitment, Progress and Track Evaluation

Trainee Candidates: Students recruited into the Biology of Breast Cancer Training Program are selected on the basis of outstanding academic credentials, a stated desire to study and conduct research in the area of breast cancer biology, and an assessment of individual research potential by the training faculty. Many of the applicants to the Mayo Graduate School have had research experience within the Mayo system through summer undergraduate research internships.

Typically, candidates for admission to Mayo's graduate programs apply directly to the Graduate School where their academic credentials, letters of recommendation, and personal statements are placed on record. Applicants are selected for on-sight interview by the Mayo Graduate School Admissions Committee. The interview process involves faculty and student assessment of each applicant's research and academic interests. The Biology of Breast Cancer Training Program also has placed special emphasis on recruitment and training of under-represented minorities. Currently the predoctoral class consists of a total of 16 students, 3 of whom are minorities (19%, including one Native American, and two Hispanic students).

Trainee Evaluation

Trainee evaluation takes place at several levels and is assessed by comparison of established and objective data relating recruitment credentials, program completion, academic performance, placement, and ultimately career achievement.

- Academic performance of trainees, including coursework evaluation and consideration of reports from the trainee's Qualifying Exam and Thesis Advisory Committees.
- Successful completion of the degree program.
- Success in gaining competitive pre- and postdoctoral fellowships and/or extramural funding.
- Ultimately, the appointment of these trainees to independent research positions with evidence of ongoing research activities relevant to cancer biology.

Curriculum and Program Evaluation

Curriculum and Program evaluation includes the areas listed below, as well as additional areas defined by the External Review Committee:

- Ability to recruit and retain outstanding Ph.D. candidates.
- Course content and appropriateness to the biology of breast cancer.
- Thoroughness of didactic and formal training in the biology of cancer.
- Effectiveness of teaching and examining methods and procedures.
- Vitality and effectiveness of student/faculty interactions in the academic components of the program.
- Evidence of faculty mentorship and establishment of intramural and extramural professional networks.
- Scope and role of individual faculty participation in the Biology of Breast Cancer Training Program.
- Integration of the clinical perspective and understanding of physician and patient concerns in the diagnosis and treatment of cancer.
- Overall effectiveness of the Program Director, Co-Director, Education Committee, and of the Graduate School in administering the Biology of Breast Cancer Training Program.

In addition to these standards to be used for self-evaluation (through surveys of both trainees and faculty), the Biology of Breast Cancer Training Program has successfully completed two rigorous external reviews, each of which has resulted in an extramural training award (i.e., the US Army Medical Research and Materiel Command award for predoctoral training in the "Biology of Breast Cancer" (DAMD17-94-J-4116), and a T32 Training Grant from the National Cancer Institute for predoctoral training in "Tumor Biology" (CA75926)). One aspect of these predoctoral awards is a requirement for formalization of an External Advisory Committee and periodic external review by this Committee.

Syllabus Outlines for Selected Tumor Biology Track Courses

Mayo Tumor Biology track courses cover a series of topics of historic relevance and primary importance to cancer biology. In addition, each year course organization and content evolve according to current trends and in order to incorporate breaking forefront issues in this dynamic field. Cancer Course syllabus outlines for 1998, indicating topic, format, and faculty are listed on the following pages.

Tumor Biology I:
Introduction to Tissue and Tumor Biology (TBIO 5000)
 2:30 - 4:00 p.m. Tue. Thur. Fall Quarter 1998
[50% participation, 25% term paper, 25% lab/problem sets]

September 29	Principles of Cell and Tissue Design	Salisbury
September 30	TBJC: Fundamentals of the Cell Cycle	
October 1	Laboratory - Light and Electron Microscopy	
October 6	Stem Cells, Differentiation, and Cancer	Maihle
October 7	TBJC: Genomic Instability/Aneuploidy	
October 8	Guest Lecture - Epigenetics and Genetics	
October 13	Properties of Transformed Cells <i>in vitro</i>	Maihle
October 14	TBJC: Temin - Hayflick	
October 15	Senescence and Immortalization	
October 20	Properties of Transformed Cells <i>in vivo</i>	Maihle
October 21	TBJC: Transgenics and Knockouts	
October 22	Xenografts	
October 27	Tissue Biology - Epithelia	Salisbury
October 28	TBJC: Cell Polarity	
October 29	Laboratory - Epithelia [TERM PAPER OUTLINE DUE by 4:00 p.m.]	
November 3	Tissue Biology - Connective Tissue	Salisbury
November 4	TBJC: Invasion and Metastasis	
November 5	Laboratory - Connective Tissue	
November 10	Endothelial Cells, Vascular Tissue and Lymphatics	Salisbury
November 11	TBJC: Angiogenesis	
November 12	Laboratory - Vascular Tissue	
November 17	Pathobiology of Cancer	Salisbury
November 18	TBJC: Epithelial / Mesenchymal Interactions	
November 19	Surgical Pathology Tours	
November 24	INDEPENDENT STUDY	
November 25	INDEPENDENT STUDY	
November 26	Thanksgiving	
December 1	Normal Breast / Breast Cancer [TERM PAPER DUE by 4:00 p.m.]	Salisbury
December 2	TBJC: Breast Tumor Staging and Grade	
December 3	Laboratory - Breast Pathology	
December 8	Normal Intestine / Colon Cancer	TBA
December 9	TBJC: HNPCC - MIN Mice	
December 10	Laboratory - GI Tumors	
December 17	[TERM PAPER EVALUATIONS DUE by 4:00 p.m.]	

Tumor Biology II:
Origins of Human Cancer (TBio 8000)
 2:30 - 4:00 p.m. Tue. Thur. Winter Quarter 1998
 [50% participation/50% term paper]

January 7	Origins of Human Cancer: An Overview	Maihle
January 8	Tumor Biology Journal Club:	
January 9	Problem Set (Maihle)	
January 14	Origins of Human Cancer: Etiology and Genetics	Smith
January 15	Tumor Biology Journal Club:	
January 16	Problem Set	
January 21	Origins of Human Cancer: Progression and Metastasis	Gendler
January 22	Tumor Biology and Journal Club: Angiogenesis	
January 23	Problem Set (Gendler and Maihle)	
January 28	Origins of Human Cancer: Epidemiology and Prevention	Yang
January 29	Tumor Biology Journal Club: Intestinal Polyposis and COX-2	
January 30	Tumor Immunology: An Overview	Mitchell
February 4	Problem Set (Epidemiology and Prevention)	
February 5	Tumor Biology Journal Club (Tumor Immunology)	Jelinek
February 6	Problem Set (Tumor Immunology)	
February 11	Paraneoplastic Syndromes (in Breast and Ovarian Cancer)	Lennon
February 12	Tumor Biology Journal Club: Paraneoplastic Autoimmunity	
February 13	Problem Set	
February 25	Introduction to Clinical Research	O'Fallon
February 26	Tumor Biology Journal Club: Phase I Trial of Dolastatin-10	
February 27	Problem Set	
March 4	Introduction to Chemotherapy	Ames
March 5	Tumor Biology Journal Club: Inhibitors of Farnesyl Transferase	
March 6	Problem Set	
March 11	Tumor Imaging: An Overview	Robb
March 12	Experimental Tumor Imaging	Ehman
March 13	Problem Set (Maihle)	
March 18	Introduction to Surgical Oncology	Nelson
March 19	Tumor Biology Journal Club: Surgical Procedures in Colon Cancer	
March 25	Introduction to Radiation Therapy	Bonner
March 26	Breast Cancer Patient Vignettes	
March 27	Experimental Gene Therapy	Raffel

Tumor Biology III

Growth Factors, Oncogenes, and Tumor Suppressors (TBIO 8005)

2:30 - 4:00 p.m. Tue. Thur. Winter Quarter 1998

[50% participation/50% term paper]

April 7	Cell Cycle and Cell Growth Control	Salisbury
April 8	Tumor Biology Journal Club	
April 9	Regulation of Immediate Early Gene Expression (AACR Meeting 3/28 - 4/1)	Getz
April 14	Growth Factors/GF Receptors	Maihle
April 15	Tumor Biology Journal Club	
April 16	Student Discussion Problem Set	
April 21	Intracellular Mediators: Kinases and Phosphatases	Maihle
April 22	Tumor Biology Journal Club	
April 23	Student Discussion Problem Set	
April 28	Intracellular Mediators: G Proteins	Karnitz
April 29	Tumor Biology Journal Club	
April 30	Student Discussion Problem Set	
May 5	Oncogenes and Viral Oncogenes	Maihle
May 6	Tumor Biology Journal Club	
May 8	Student Discussion Problem Set	
May 12 -14	INDEPENDENT STUDY	
May 19	Introduction to Tumor Suppressors	James
May 20	Tumor Biology Journal Club	
May 21	Student Discussion Problem Set	
May 26	Cancer Genetics	Jenkins/Lloyd
May 27	Tumor Biology Journal Club	
May 28	Student Discussion Problem Set	
June 2	P53 - Guardian of the Genome	James
June 3	Tumor Biology Journal Club	
June 4	Student Problem Set	
June 9	Retinoblastoma and Rb	Smith
June 10	Tumor Biology Journal Club	
June 11	Student Discussion Problem Set	
June 16	To Die Or Not To Die - Apoptosis	TBA
June 17	Tumor Biology Journal Club	
June 18	Student Discussion Problem Set	

Biology of Breast Cancer

(TBiol 5200)
Guggenheim 1093
1:30-2:30 p.m. Fridays

(50% participation/50% final exam)

- This course is aimed at integrating basic concepts in developmental, cellular and molecular biology of the breast together with current information on the etiology, diagnosis and treatment of breast cancer.
- The faculty include members from diverse basic science and medical disciplines including cell and molecular biology, pathology, oncology and surgery.

April 11	Breast Cancer: The Magnitude of the Problem	Ingle
April 18	Development, Anatomy and Histology and Cell Biology of the Breast	Salisbury
April 25	Histopathology of the Breast	Wold
May 2	Experimental Models of Breast Cancer	Gendler
May 9	Oncogenes, Growth Factors, and Breast Cancer	Leof
May 16	Tumor Suppressors and Breast Cancer	Mr. Ritland
May 23	Radiation Therapy for Breast Cancer	Peterson
May 30	Surgical Treatment of Breast Cancer	Donohue
June 6	Breast Cancer Diagnosis and Imaging	Johnson
June 13	Systemic Therapy for Breast Cancer	Ingle
June 20	Experimental Therapies for Breast Cancer	Maihle
June 27	Final Examinations Due (by 5:30 p.m.)	

Business of Science, Science of Business

TBio 5300

K. E. Bennet, M.B.A. and N. J. Maihle, Ph.D.

Summer Quarter (even years)

- 1) Introduction (August 2) Orientation and Objectives [KEB/NJM]
- 2) Administrative Structures in Support of Research (August 5) [KEB]
Not-for-Profit & For Profit
- 3) Overview of Research Accounting (August 7) [KEB]
Research Budgets
Direct versus Indirect costs
- 4) Sources of Financial Support for Research (August 9) [NJM]
Intramural & Extramural Support
Federal & Private
- 5) Sources of Financial Support for Research (August 12) [KEB]
Corporate
Strategic Alliance, Joint Development
Licensing/Venture Capital
- 6) Introduction to Intellectual Property (August 14) [KEB]
Definition of Intellectual Property
Protection of Intellectual Property
Patents & Trade Secrets
Ownership of Intellectual Property
- 7) Introduction of Cases (August 16) [KEB]
- 8) Commercialization of Research Discoveries (August 21) [KEB]
Licensing
Market Value of Invention
- 9) Independent Study on Cases (August 19)
- 10) Laws and Policies Governing Conduct of Research (August 23)
Institutional [NJM]
State, Federal, and International [KEB]
- 11) Case Presentations "Levamisole" (August 26) [KEB/NJM]
- 12) Case Presentations - "University of Florida" (August 28) [KEB/NJM]
- 13) Course Wrap-Up (August 30) [KEB/NJM]

Current Topics in Tumor Biology

(TBiol 5151)
2:30 - 3:30 p.m. Wednesdays

Journal Club Topics and (Presenter) Academic Year 1997-1998

- 10/1 Expression genetics in cancer: Shifting the focus from DNA to RNA. Ruth Sager (1997) *Proc. Natl. Acad. Sci. USA* 94: 952-955.
Expression of maspin in prostate cells is regulated by a positive Ets element and a negative hormonal responsive element site recognized by androgen receptor. Ming Zhang, David Magit, and Ruth Sager (1997) *Proc. Natl. Acad. Sci. USA* 94: 5673-5678 (Ms. Julie Johnson)
- 10/8 Normal genetically mosaic mice produced from malignant teratocarcinoma cells. Beatrice Mintz and Karl Illmensee (1975). *Proc. Natl. Acad. Sci. USA* 72: 3585-3589.
Successive generations of mice produced from an established culture line of euploid teratocarcinoma cells. Timothy Stewart and Beatrice Mintz (1981) *Proc. Natl. Acad. Sci. USA* 78: 6314-6318 (Mr. Michael Rogers)
- 10/15 The Werner syndrome protein is a DNA helicase. Gray, Shen, Kamath-Loeb, Blank, Sopher, Martin, Oshima, and Loeb, (1997). *Nature Genetics* 17:100-103.
(Ms. Nohelia Canales)
- 10/22 Differences between the ribonucleic acids of transforming and nontransforming avian tumor viruses. P.H. Duesberg and P.K. Vogt (1970) *Proc. Natl. Acad. Sci. USA* 67:1673-1680.
DNA related to the transforming gene(s) of avian sarcoma viruses is present in normal avian DNA. D. Stehelin, H.E. Varmus, J.M. Bishop, P.K. Vogt (1976) *Nature* 260:170-173.
Transformation of chicken cells by the gene encoding the catalytic subunit of PI3-kinase. Chang, et al., (1997, *Science* 276:1848-1850)
(Mr. Eric Calhoun)
- 10/28 Life and Cancer Without Telomerase. V.A. Zakian (1997) *Cell* 91:1-3.
Telomere shortening and tumor formation by mouse cells lacking telomerase RNA. M.A. Blasco et al., (1997) *Cell* 91:25-34. (Ms. Colleen Schehl)
- 11/12 Embryonic lethality and radiation hypersensitivity mediated by Rad51 in mice lacking Brca2. Sharan et al., (1997) *Nature* 386:804-810.
Targeted mutations of breast cancer susceptibility gene homologs in mice: lethal phenotypes of Brca1, Brca2, Brca1/Brca2, Brca1/p53, and Brca2/p53 nullizygous embryos. Ludwig et al., (1997) *Genes and Development* 11:1226-1241.
Brca2 is required for embryonic cellular proliferation in the mouse. Suzuki et al., (1997) *Genes and Development* 11:1242-1252.
(Dr. Cecelia Boardman)
- 11/19 Regulation of gene expression by small molecules. Gottesfeld et al., (1997) *Nature* 387:202-205.
Discrimination of 5'-GGGG-3', 5'-GCGC-3', and 5'-GGCC-3' sequences in the minor groove of DNA by eight-ring hairpin polyamines. Swalley et al., (1997) *J. Amer. Chem. Soc.* 119:6953-6961.

Recognition of seven base pair sequences in the minor groove of DNA by ten-ring pyrrole-imidazole polyamide hairpins. Turner et al., (1997) *J. Amer. Chem. Soc.* 119:7636-7644.
(Ms. Gwen Lomberg)

- 1/14 The role of histological grading in the prognosis of patients with carcinoma of the breast. N.E. Roberti, (1997). *Cancer* 80:1708-1716.
Histological grade as a prognostic factor in breast carcinoma. H. Burke and D.E. Henson, (1997) *Cancer* 80:1703-1705.
Consensus conference on the classification of ductal carcinoma *in situ*. G. Schwartz et al., (1997) *Cancer* 80:1798-1802.

(Ms. Colleen Schehl)

- 1/21 Suppression of glioblastoma angiogenicity and tumorigenicity by inhibition of endogenous expression of vascular endothelial growth factor. S-Y. Cheng et al, (1996). *Proc. Natl. Acad. Sci.* 93:8502-8507.
Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1 mutant. B. Millauer et al., (1994). *Nature* 367:576-578.

(Ms. Julie Johnson)

- 1/28 Localization of Kaposi's sarcoma-associated herpesvirus in bone marrow biopsy samples from patients with multiple myeloma. J.W. Said, et al., (1997). *Blood* 90:4278-4282.
Kaposi's sarcoma-associated herpesvirus infection of bone marrow dendritic cells from multiple myeloma patients. M.B. Rettig et al., (1997). *Science* 276:1851-1854.
Kaposi's sarcoma-associated herpesvirus infection and multiple myeloma. C. Parravicini et al., (1997). *Science* 278: 1969-1973.
HHV-8 and multiple myeloma in France, and the UK. A-G Marcelin et al., and MacKenzie et al., (1997). *The Lancet* 350:603-604.

(Mr. Andy Danielsen)

- 2/4 Recent Advances in Chemoprevention of Cancer. W.K. Hong and M.B. Sporn, (1997). *Science* 278:1073-1077.
Tamoxifen Breast Cancer Prevention Trial - An Update. L.G. Ford and K.A. Johnson (1997). in: *Etiology of Breast and Gynecological Cancers*. Wiley-Liss Inc. pages 271-282.

(Mr. Kun Xu)

- 2/25 Natural History of Cervicovaginal Papillomavirus Infection in Young Women. G.Y.F. Ho et al., (1998). *New Engl. J. Med.* 338:423-428.
HPV Infection in Women Infected with the Human Immunodeficiency Virus. X.W. Sun et al., (1997). *New Engl. J. Med.* 337:1343-1349.
HPV and Anogenital Cancer. K.V. Shah (1997). *New Engl. J. Med.* 337:1386-1388.
Genetic Alterations Accumulate during Cervical Tumorigenesis and Indicate a Common Origin for Multifocal Lesions. A.A. Larson et al., (1997). *Cancer Research* 57:4171-4175.

(Ms. Gwen Lomberg)

- 3/4 Regulated expression of the diphtheria toxin A chain by a tumor-specific chimeric transcription factor results in selective toxicity for alveolar rhabdomyosarcoma cells. E.S. Massuda et al., (1997). *Proc. Natl. Acad. Sci. USA.* 94:14701-14706.
Chromosomal translocations in human cancer. T.H. Rabbitts (1994). *Nature* 372:143-149.

(Mr. Eric Calhoun)

- 3/11 The Yin and Yang of T Cell Costimulation. J.P. Allison and M.F. Krummel, (1995). *Science* 270:932-933.
Enhancement of Antitumor Immunity by CTLA-4 blockade. D.R. Leach, M.F. Krummel, AND J.P. Allison, (1996). *Science* 271:1734-1736.
(Mr. Jonathan Hoyne)
- 3/18 Conservation of the Chk1 Checkpoint Pathway in Mammals: Linkage of DNA Damage to Cdk Regulation Through Cdc25. Y. Sanchez et al., (1997). *Science* 277:1497-1501.
Mitotic and G2 Checkpoint Control: Regulation of 14-3-3 Protein Binding by Phosphorylation of Cdc25C on Serine-216. C.-Y. Peng et al., (1997). *Science* 277:1501-1505.
(Mr. Kurt Krummel)
- 3/25 p53-Dependent Apoptosis Modulates the Cytotoxicity of Anticancer Drugs. S.W. Lowe, E.H. Ruley, T. Jacks, and D. Housman, (1993). *Cell* 74:957-967.
Uncoupling of S Phase and Mitosis Induced by Anticancer Agents in Cells Lacking p21. T. Waldman, C. Lengauer, K. Kinzler, and B. Vogelstein, (1996). *Nature* 381:713-716.
(Ms. April Blajeski)
- 4/8 Splicing into Senescence: The Curious Case of p16 and p19^{ARF}. Daniel A. Haber (1997). *Cell* 91:555-558.
Tumor Suppression at the Mouse INK4a Locus Mediated by the Alternative Reading Frame Product p19^{ARF}. T. Kamijo, et. al., (1997). *Cell* 91:649-659.
(Dr. Jill Reiter)
- 4/15 Trans receptor inhibition of human glioblastoma cells by erbB family ectodomains. D.M. O'Rourke et al., (1997). *Proc. Natl. Acad. Sci.* 94:3250-3255.
The enhanced tumorigenic activity of a mutant epidermal growth factor receptor common in human cancers is mediated by threshold levels of constitutive tyrosine phosphorylation and unattenuated signaling. H-J. Su Huang et al., (1997). *J. Biol. Chem.* 272:2927-2935.
(Mr. Jonathan Hoyne)
- 4/22 Matrix adhesion and Ras transformation both activate a phosphoinositide 3-OH kinase and protein kinase B/Akt cellular survival pathway. A. Khwaja et al., (1997). *EMBO* 16:2783-2793.
(Mr. Kun Xu)
- 4/29 A serine/threonine kinase gene defective in Peutz-Jeghers syndrome. A. Hemminki et al., (1998). *Nature* 391:194-186.
Cloning and characterization of a novel serine/threonine protein kinase expressed in early *Xenopus* embryos. J-Y Su et al., (1996). *J. Biol. Chem* 271:14430-14437.
(Ms. Susan Barrett)
- 5/6 Forced degradation of Fas inhibits apoptosis in adenovirus-infected cells. A.E. Tollefson et al., (1998). *Nature* 392:726-730.
(Dr. Cecelia Boardman)
- 5/20 Serial Analysis of Gene Expression. V. Velculescu, L. Zhang, B. Vogelstein, and K. Kinzler (1995). *Science* 270:484-487.
Gene Expression Profiles in Normal and Cancer Cells. L. Zhang, W. Zhou, V. Velculescu, S. Kern, R. Hruban, S. Hamilton, B. Vogelstein, and K. Kinzler (1995). *Science* 276:1268-1272.
(Mr. Eric Calhoun)

- 5/27 Involvement of *Brca2* in DNA Repair. K.J. Patel et. al., (1998). *Molecular Cell* 1: 347-357.
Tumorigenesis and a DNA repair defect in mice with a truncating *Brca2* mutation. F. Connor et. al., (1998). *Nature Genetics* 17:423-430-1272.
(Ms. Colleen Schehl)
- 6/3 Kinetochore Localization of Murine Bub1 is Required for Normal Mitotic Timing and Checkpoint Response to Spindle Damage. S. Taylor and F. McKeon, (1997). *Cell* 89: 727-735.
Mutations of Mitotic Checkpoint Genes in Human Cancers. D. Cahill et. al., (1998). *Nature* 392:300-303.
(Mr. Andrew Danielson)
- 6/10 Replacement of Fhit in cancer cells suppresses tumorigenicity . Z. Siprashvili et al., (1997). *Proc. Natl. Acad. Sci.* 94:13771-13776.
Genetic, biochemical, and crystallographic characterization of Fhit-substrate complexes as the active signaling form of Fhit . H.C. Pace et. al., (1998). *Proc. Natl. Acad. Sci.* 95:5484-5489.
(Ms. Gwen Lomberg)
- 12/12 **Special Seminar:** The Findling Lecture. "Tumor Angiogenesis"
(Dr. Judah Folkman)

Biology of Breast Cancer Program Extramural Training Support

<u>Grant #</u>	<u>P.I.</u>	<u>Source</u>	<u>Term</u>	<u>Total Direct</u>
T32 CA 75926	Salisbury, J.L.	NCI	7/1/98-6/30/03	\$805,414
	Biology of Cancer: A Predoctoral Training Program			
DAMD J-4116-3	Maihle, N.J.	US Army	9/1/94-8/31/98	\$370,154
	Biology of Breast Cancer: A Predoctoral Training Program			
NRSA	Baines, J.E.	NIH	9/15/97-5/31/02	
	Novel Immunotherapeutic Approaches to Cervical Cancer			
NRSA	Canales, N.D.	NIH	5/1/97-5/1/02	
	Research Training in Breast and Ovarian Cancer			

Program Trainees

<u>Name</u>	<u>Date Entered</u>	<u>Research Mentor</u>	<u>Qualifying Examination</u>	<u>Thesis Defense</u>
Baines, Jonathan	6/3/96	Dr. Persing	passed	
Calhoun, Eric	7/7/97	(rotations)		
Canales, Nohelia	1/6/97	Dr. Gendler		
Eley, Gregory	7/8/96	Dr. James		
Holmen, Sheri	9/5/95	Dr. Federspiel	passed	
Johnson, Julie	7/8/96	Dr. Maihle		
Lomberg, Gwen	8/6/97	Dr. Smith		
Ritland, Steve	7/1/96	Dr. Gendler	passed	7/98
		"Strain dependent modulation of mammary tumor latency and phenotype in C-erbB2 transgenic mice."		
Rogers, Michael	8/16/93	Dr. Strehler	passed	
Schehl, Colleen	8/4/97	Dr. Couch		
Xu, Kun	6/18/97	Dr. Prendergast		
Melissa Adriance	8/1/98	(pending entry)		
Jessica Faupel	7/1/98	(pending entry)		
Shannon Myers	6/1/98	(rotations)		
Denise Walters	6/1/98	(rotations)		

Student Highlights:

Steve Ritland (Dr. Gendler's laboratory) has completed all track requirements. He is nearing completion of his thesis work, and he will to defend his thesis July 10 of 1998. Steve's thesis project includes a study entitled: "Strain dependent modulation of mammary tumor latency and phenotype in C-erbB2 transgenic mice." He is presently exploring postdoctoral positions in several high caliber cancer research laboratories.

Sheri Holmen (Dr. Federspiel's laboratory) has completed all track course requirements and her qualifying examination. Her research on retroviral vectors and soluble receptors is progressing well. Sheri is also an active member of the Mayo Graduate School Education Committee: during January she conducted an extensive survey and analysis of graduate student opportunities for extramural funding for the Mayo Graduate School. Sheri completed the AACR workshop on "Histopathology of Neoplasia" during the summer of 1997.

Mike Rogers (Dr. Strehler's laboratory) has completed his qualifying examination and course requirements, and has recently identified CLP-binding proteins using the yeast two hybrid screen. Completion of this work will complement his earlier studies on CLP expression in human breast tumors, and these studies will serve as a basis for his thesis. Mike completed the AACR workshop on "Histopathology of Neoplasia" during the summer of 1995.

Jonathan Baines (Dr. Persing's laboratory) has completed his course requirements and qualifying examination and has recently begun his thesis studies on the utility of HPV antigens as potential cervical cancer vaccines. Jon was awarded an NIH NRSA Fellowship based on his research proposal on "Novel Immunotherapeutic Approaches to Cervical Cancer", and he presented an overview of this project in the Tumor Biology Interest Group (TBIG) in March. Jon is an active member of the Training Program Education Committee

Nohelia Canales (Dr. Gendler's laboratory) is completing her final coursework and is just initiating her thesis research on Muc-1 expression in normal tissue and mammary tumors using the transgenic and knockout mouse models. Nohelia was awarded an NIH NRSA fellowship based on training in the Tumor Biology Program, and recently received an AACR Travel Award for her participation in this year's AACR meeting.

Greg Eley (Dr. James' laboratory) is completing his coursework and will take his qualifying examination during the Summer Quarter. He has recently submitted a first author manuscript for publication describing a novel transcript that is co-amplified with the ErbB1 gene. Greg is enrolled in the *Genome Analysis* course to be held at Cold Spring Harbor Laboratory and the *Medical and Experimental Genetics* course to be held at the Jackson Laboratory this summer.

Julie Johnson (Dr. Maihle's laboratory) has completed her coursework and will take the qualifying examination during the Summer Quarter. Her thesis project is on track and she has completed her first thesis advisory committee meeting. Julie's thesis project is a study of alternate erbB signalling pathways. Julie completed the AACR workshop on "Histopathology of Neoplasia" during the summer of 1997. Julie also has served as the student representative to the Graduate School's Admissions committee this past year.

1997-1998 freshman trainees include: **Eric Calhoun, Gwen Lomberg, Colleen Schehl, and Kun Xu.** Colleen Schehl has begun work in her thesis laboratory with Dr. Fergus Couch studying BRCA2 - p53 interactions. 1998-1999 entering trainees include: **Melissa Adriance, Jessica Faupel, Shannon Myers, and Denise Walters.**

THE FACULTY AND THEIR RESEARCH

Tumor Biology Program

- Robert T. Abraham, Associate Professor; Ph.D., Pittsburgh, 1981. Signal transduction; cell-cycle regulation; leukemogenesis.
- Matthew M. Ames, Professor; Ph.D., California, San Francisco, 1976. Development and characterization of novel antitumor agents.
- Amy G. Andrews, Assistant Professor; D.V.M., Michigan State, 1987. Animal models in cancer studies.
- Margot P. Cleary, Visiting Scientist; Ph.D., Columbia, 1976. Breast cancer; obesity; nutrition.
- Fergus J. Couch, Assistant Professor; Ph.D., University College Cork, Ireland, 1992. Identification and characterization of genes involved in familial and sporadic breast and ovarian cancer development. Functional analysis of the BRCA2 breast and ovarian cancer predisposition gene.
- Chella S. David, Professor; Ph.D., Iowa State, 1966. Immunogenetic aspects of immune response, with emphasis on the major histocompatibility complex class II Ia genes and T-cell receptor gene.
- Gordon W. Dewald, Professor; Ph.D., North Dakota, 1972. Cytogenetics and molecular cytogenetics of congenital disorders and hematologic malignancies.
- Richard L. Ehman, Professor; M.D., Saskatchewan, 1979. Magnetic resonance imaging.
- Charles Erlichman, Professor; M.D., Toronto (Canada), 1974. Pharmacology of drugs used in cancer therapy.
- Mark J. Federspiel, Assistant Professor; Ph.D., Michigan State, 1987. Retroviral vectors; antiviral strategies; molecular medicine.
- Lorraine A. Fitzpatrick, Professor; M.D., Chicago, 1980. Prostate cancer metastatic to bone; skeletal calcification; steroid regulation of metastatic disease.
- *Sandra J. Gendler, Associate Professor; Ph.D., USC, 1984. Tumor cell biology; mucins in cancer and cystic fibrosis.
- Michael J. Getz, Professor; Ph.D., Texas at Houston, 1972. Molecular biology of peptide growth factors; biology of tissue factor in tumorigenesis.
- Joseph P. Grande, Associate Professor; Ph.D., 1983, M.D., 1985, Chicago. Extracellular matrix and breast cancer; tumor pathology.
- James N. Ingle, Professor; M.D., Johns Hopkins, 1971. Clinical trials, hormonal therapy, and prognostic/predictive factors in breast cancer.
- C. David James, Associate Professor; Ph.D., Wright State, 1986. Cancer genetics; cell cycle regulation.
- Diane F. Jelinek, Assistant Professor; Ph.D., Texas Southwestern Medical Center, 1985. Cytokine-mediated signaling and gene expression in normal and malignant human B lymphocytes.
- Robert B. Jenkins, Associate Professor; Ph.D., 1981, M.D., 1983, Chicago. Genetics of brain, prostate and women's cancer.
- Larry M. Karnitz, Assistant Professor; Ph.D., Iowa, 1989. Signaling mechanisms of oncogenes and hemopoietic growth factors; molecular radiobiology.
- Scott H. Kaufmann, Associate Professor; M.D./Ph.D., Johns Hopkins, 1981. Pharmacology of topoisomerase-directed antineoplastic agents; apoptosis; resistance to anticancer drugs.
- Paul J. Leibson, Associate Professor; Ph.D., 1981, M.D., 1979, Chicago. Tumor immunology; lymphocyte activation; antiviral immunity.
- Vanda A. Lennon, Professor; M.B.B.S., Sydney (Australia), 1966; Ph.D., Melbourne (Australia), 1973. Immunobiology of autoimmunity and cancer; ionic channel protein antigens in human neoplasms of lung, ovary, and breast (carcinomas), and thymic epithelium (thymoma).
- Edward B. Leof, Associate Professor; Ph.D., North Carolina, 1982. Regulation of cellular proliferation; genetics of pneumocystis carinii.
- Ricardo V. Lloyd, Professor; M.D./Ph.D., Wisconsin, Madison, 1975. Endocrine tumor biology, especially pituitary and thyroid.

- John A. Lust, Assistant Professor; M.D./Ph.D., Boston University, 1983. Role of IL-6 and IL-6R in pathogenesis of multiple myeloma; detection of minimal residual disease in myeloma transplant patients by PCR.
- L. James Maher, Associate Professor; Ph.D., Wisconsin, 1988. Nucleic acid biochemistry; triple helix DNA.
- Nita J. Maihle, Associate Professor; Ph.D., Yeshiva (Einstein), 1983. Molecular basis of cancer; human breast, ovarian, and prostate carcinomas; gliomas.
- David J. McKean, Professor; Ph.D., Johns Hopkins, 1972. Signaling and gene transcription events in T helper lymphocytes; MHC class II protein transport.
- Michael J. McManus, Assistant Professor; M.D., Georgetown, 1983. Molecular pediatric oncology; growth factor receptors; tyrosine kinase signal transduction pathways.
- Mark A. McNiven, Associate Professor; Ph.D., Maryland, 1987. Cytoskeletal dynamics in mammalian cells; molecular basis of cellular migration during metastasis; vesicle-based transport in epithelial cells.
- L. Joseph Melton, III, Professor; M.D., LSU, 1969. Chronic disease epidemiology.
- Heidi Nelson, Associate Professor; M.D., Washington (Seattle), 1981. Colorectal cancer; immunotherapy.
- Judith R. O'Fallon, Professor; Ph.D., North Carolina, 1973. Cancer clinical trials design, conduct, and analysis.
- Dennis J. O'Kane, Assistant Professor; Ph.D., SUNY at Stony Brook, 1979. Telomerase activity as a diagnostic marker for cancer; translational research on new tumor markers.
- David H. Persing, Associate Professor; M.D./Ph.D., California, San Francisco, 1988. Precore promoter mutations in hepatic tumors; immunogenetic determinants of chronic papillomavirus infections and cervical cancer; association of chronic infections with lymphoproliferation.
- Mark R. Pittelkow, Professor; M.D., Mayo, 1979. EGF-related growth factor/receptor function: epidermal keratinocyte and melanocyte regulation of growth and differentiation.
- Karl C. Podratz, Professor; M.D./Ph.D., St. Louis, 1974. Molecular prognostic determinants in gynecologic malignancies.
- Gregory A. Poland, Professor; M.D., Southern Illinois. Expertise in vaccine development and evaluation, adjuvant development and evaluation; vaccine antigen processing and HLA presentation; and vaccine immunogenetics.
- Franklyn G. Prendergast, Professor; M.B.B.S., West Indies, 1968; Ph.D., Minnesota, 1977. Fluorescence spectroscopy; protein structure and dynamics; biochemistry and bioluminescence.
- Corey Raffel, Associate Professor; M.D./Ph.D., California, San Diego, 1980. Pediatric neuro-oncology; gene therapy and cancer.
- Jeffrey L. Salisbury, Professor; Ph.D., Ohio State, 1978. Cell cycle control; centrosomes; mitotic spindle poles; breast cancer.
- David I. Smith, Professor; Ph.D., Wisconsin, 1978. Chromosomal fragile sites; molecular genetics of cancer development.
- Thomas C. Spelsberg, Professor; Ph.D., West Virginia, 1967. Steroid action on early (*c-myc*) gene transcription, steroids and TGF- β action on bone cell functions, and early gene expression.
- Emanuel E. Strehler, Associate Professor; Ph.D., ETH Zurich (Switzerland), 1981. Intracellular Ca^{2+} homeostasis and signaling; molecular mechanisms of disease.
- Stephen N. Thibodeau, Professor; Ph.D., Washington (Seattle), 1979. Cancer genetics; colon and prostate cancer.
- Donald J. Tindall, Professor; Ph.D., North Carolina, 1973. Mechanism of androgen action in prostate cancer.
- David O. Toft, Professor; Ph.D., Illinois, 1967. Mechanisms of action of steroid receptors and heat shock proteins.
- Raul Urrutia, Assistant Professor; M.D., Cordoba (Argentina), 1987. Cell differentiation.
- Richard M. Weinshilboum, Professor; M.D., Kansas, 1967. Molecular pharmacogenetics of drug metabolism - including antineoplastic agents.

Peter J. Wettstein, Professor; Ph.D., North Carolina at Chapel Hill, 1977. Role of minor histocompatibility antigens in allograft rejection.
Anthony J. Windebank, Professor; B.M. B.Ch., Oxford, 1974. Molecular mechanisms of neurotoxic cell injury; growth factors and regeneration.
Lester E. Wold, Professor; M.D., Chicago, 1977. Immunocytochemistry; bone tumors and tumor-like conditions; breast diseases.
Charles Y-F. Young, Assistant Professor; Ph.D., Brigham Young, 1984. Calpain inhibitor-induced apoptosis in human prostate adenocarcinoma cells.

*Scottsdale campus.

Research and Resource Facility Information Sheet

Mayo Research Facilities

The research training environment and research facilities at Mayo are exceptional. There are approximately 150 career scientists and clinicians engaged in research at Mayo, along with their associated research personnel. The annual Mayo research budget is approximately \$140 million, which is derived in roughly equal proportions from extramural and Mayo Foundation funds. In 1997, approximately two-thirds of Mayo's extramural support was provided through grants and contracts awarded through the National Cancer Institute. Thus, research at Mayo is both well supported by the institution and recognized for its excellence through a competitive extramural peer-review process. Internal research resources are administrated by the Mayo Foundation Research Committee (Rochester) and the Mayo Cancer Center Advisory Committee.

Mayo Core Facilities

The Mayo Foundation supports most major research instrumentation needs, and, in addition, provides resources required for shared equipment core facilities. These include 10 'core' research laboratories that serve as major scientific and educational resources for students and their respective laboratories. Each Shared Mayo Research Resource is overseen by a Mayo staff investigator with expertise in the appropriate area in addition to a staff of professional research assistants who are expert in the use of instrumentation specific for the particular facility. Faculty and students can access these resources at many levels. An 'occasional' use or analysis can be performed by the facility staff. Students whose research projects require more extensive use of a facility can be trained by the technical staff in a given facility and, thereby, develop technical expertise themselves. Thus, students can truly follow their research question wherever it may take them, even if it goes beyond the technologies available in their mentor's laboratory.

Mayo Clinic Shared Research Resource Facilities.

Analytical NMR Resource	Biomedical Imaging Resource
Electron Microscopy Resource	Flow Cytometry/Optical Morphometry
Mass Spectroscopy Resource	Mathematical Methods Resource
Molecular Biology Resource	Protein Sequencing/Peptide Synthesis
Radioimmunoassay Resource	Research Computing Facility
Pharmacology Core	Cytogenetics Core
Cancer Biostatistics Core	Pathology Core

Analytical nuclear Magnetic Resonance Facility (NMR) - (625-341-9800)

Dr. S. Macura, Director (4-6937). Analytical Nuclear Magnetic Resonance Facility supports applications of high-field nuclear magnetic resonance (NMR) spectroscopy to biochemical and biological systems, in particular, structure-function studies of biomacromolecules. The facility contains high-field state-of-the-art NMR spectrometers and computers for processing and analyzing NMR data. The facility is staffed by experts in various fields of NMR experimentation who carry out core research and development and spend part of their time consulting with and training users. Facility staff may collaborate with users who have projects of mutual interest.

Biomedical Mass Spectrometry Facility (BMSF) - (625-025-9800)

Dr. S. Naylor, Director (4-5220; pager 4-6091) Additional Contact Person - Dr. A. J. Tomlinson (4-1040; pager 4-7506). The Biomedical Mass Spectrometry Facility is a resource for Mayo investigators to isolate and structurally characterize a wide range of biological relevant compounds. The activities within the BMSF are focused on four specific services; 1) Consultation and education involving the isolation and characterization of biopolymers and metabolites; 2) Routine molecular weight service of molecules including biopolymers, metabolites, and lipids; 3) CE and HPLC separation of complex mixtures; and 4) long-term collaborative interactions with Mayo investigators involving the isolation and structural characterization of biopolymers and metabolites from complex biological matrices.

Electron Microscopy Core Facility (EMCF) - (625-347-9800)

Dr. J. L. Salisbury, Director (4-3326) Additional Contact person - Jon Charlesworth (4-3148 or 4-1616). The Electron Microscopy Core Facility provides specimen preparation, microscopy, and photography services to investigators from both clinical and basic science laboratories. In addition to standard transmission and scanning electron microscopy, the facility performs x-ray probe microanalysis and immuno-gold labeling procedures.

Flow Cytometry/Optical Morphology Core Facility - (625-350-9800)

Dr. P. J. Leibson, Director (4-4866) Additional Contact Person - Jim Tarara (127-0183 or 4-4241). Instrumentation of flow cytometry/cell sorting is provided for high speed cell analysis and cellular fractionation. Samples are prepared in the investigator's laboratory and can be run by core facility personnel. Complete image analysis software is available. Other instruments and services provided include confocal microscopy and computer controlled ratio imaging.

Immunochemical Laboratory Core Facility (ICL) - (560-091-9800)

Dr. G. G. Klee, Director (4-8213; pager 4-7406) C. M. Schimek, Supervisor (5-4772; pager 127-4046) Technical Coordinator - Don Heser (5-7855). The Immunochemical Core Laboratory (ICL) is a Mayo Research Committee core facility for providing laboratory testing at minimal cost to Mayo researchers. When capacity is available, testing is also provided for investigators outside Mayo on a collaborative basis and for MML clinical trials clients. The ICL staff is actively involved in new assay development and improvement of current assay methodology. The laboratory is located at 5-223 Joseph, Saint Mary's Hospital, next to the GCRC. Requests for ICL service are prioritized based on volume, number of protocols requiring the test(s), availability of an alternative source for testing and development effort required. First priority for laboratory testing is given to GCRC protocols and other NIH funded protocols.

Material and Structural Testing Resource (MSTR) - (409-103-9900)

Dr. K-N An, Director (4-2589) Additional Contact Person - Tricia Neale (4-1460). The MSTR is a facility designed to thoroughly assess the mechanical characteristics of a multitude of engineering and biologic materials. The facility is capable of developing custom tailored solutions to analyze a wide array of problems utilizing both experimental and theoretical approaches.

Biomathematics Resource - (640-151-9800)

Drs. Z. Bajzer (4-8584) and A. Manduca (4-8163), Directors. The Biomathematics Resource was established to provide advanced mathematics and computing expertise to research programs and to the Mayo community as a whole. The facility is staffed by experts in mathematical modeling, image processing, and machine learning algorithms who carry out research and development, collaborate, and provide consulting. Services provided include: 1) collaboration with Mayo investigators and/or clinicians on specific projects which require advanced mathematical and/or computational methods, 2) development of new methodologies, 3) consultation and education in mathematical and computational methods, and 4) custom development of software for specific needs.

Mayo Biomedical Imaging Resource (BIR) - (640-193-9800)

Dr. R. A. Robb, Director (4-4937; pager 4-7744) Additional contact persons: Mahlon Stacy (4-6174), Dennis Hanson (4-6103) Jon Camp (4-3870). The Mayo Biomedical Imaging Resource (BIR) is dedicated to the advancement of research in the biomedical imaging and visualization sciences. The BIR provides expertise, advanced technology and comprehensive software related to biomedical imaging and scientific visualization, including image display, processing and analysis; image databases; virtual reality; computer graphics; video animation; computer workstations; computer networks; and computer programming. The BIR also provides specialized services in computer maintenance and back-up, custom software development and imaging system design.

Mayo Protein Core Facility - (625-288-9800)

Dr. D. J. McCormick, Director (4-4992) Additional Contact Person: Benjamin Madden (4-2457). The Mayo Protein Core Facility is a resource which provides services and methods related to the isolation, characterization, and analysis of proteins. Current services provided by the facility include: 1) N-terminal amino acid sequencing; 2) Carboxyl (C) terminal sequencing; 3) amino acid analysis; 4)) protein isolation by conventional liquid chromatography (FPLC); 5) solid phase peptide synthesis at both small and large scales; 6) production of peptide immunogens by conjugation to protein carriers and MAP resins; 7) peptide nucleic acid synthesis (PNA); 8) proteolysis and peptide mapping. 9) peptide purification by reverse phase HPLC; 10) analysis of protein sequences from data bases for structural homology, synthetic peptide design, and molecular modeling For a complete description of the facility and its services use the local Web page at the site address: <http://www-rcf.mayo.edu/protein/>.

Molecular Biology Core - (625-205-9800)

Dr. B. C. Kline, Director (4-7489); Additional Contact persons: oligonucleotides - Maryjane Doerge (4-8186), DNA sequencing - Bruce Eckloff (4-3797), training - Ross Aleff (4-3794). The Molecular Biology Core synthesizes oligonucleotides, performs semi-automated, fluorescence-based DNA sequencing, and provides laboratory training in molecular biological techniques. For more information, use the local Web page <http://www-rcf.mayo.edu/molecular/>.

Research Computing Facility (RCF) - (653-000-9800)

Dr. R. A. Ghanbari, Director (4-1817) Additional contact person: Robert Bleimeyer (127-4656). The goal of the Research Computing Facility is to guide, coordinate, and enable the effective use of computing and information management technologies by the Mayo investigator. Resources available consist of a staff of computing professionals well versed in addressing the needs and interests of research using hardware and software tailored to the needs of the investigator. Five integrated services are available which include: 1) collaborative consulting; 2) education on the application of computing technology; 3) management and coordination of computing resources; 4) services for desktop computers in cooperation with other Mayo service groups; and 5) shared hardware, software, and reference data resources.



The Vanderbilt Cancer Center

Maihle, N.J.

Appendix M

A National Cancer Institute-Designated Cancer Center

649 Medical Research Building II
Nashville, Tennessee 37232-6838
Telephone: (615) 936-1782
Fax: (615) 936-1790

June 26, 1998

Nita J. Maihle, Ph.D.
Department of Biochemistry and Molecular Biology
Mayo Foundation
200 First Street SW
Rochester, Minnesota 55905

Dear Nita:

This is a response to your request for an evaluation of your predoctoral training program in breast cancer research supported by a USAMRDC training grant. I do have significant familiarity with predoctoral training programs. I have been chair of a basic science department and thus responsible for a predoctoral training program for the past 19 years and director of a National Cancer Institute training grant supporting predoctoral trainees for almost the same length of time.

From my review of the submitted materials, it is clear that you have successfully used this award to initiate a multidisciplinary training program with a particular focus in breast cancer. The administrative structure, governance and didactic course work is appropriate for training scientists to pursue breast cancer research. You have a very competitive, interactive faculty representing sufficient breadth and depth in areas relevant to breast cancer research. The best measure of a training program is the long term success of its trainees. This is difficult to evaluate in such a brief time after its initiation. However, it appears that you have been successful in recruiting excellent students, most of whom are progressing well in the program. I have had the opportunity to meet one of your trainees, Steve Ritland, who is nearing completion of his predoctoral training. He is truly impressive and shows promise for developing into an outstanding independent investigator. If you are able to produce a few more as impressive as Steve Ritland, your program will be an unqualified success.

Overall, your program has been successful in accomplishing the goals of the original US Army Breast Cancer Integration Panel of which I was a member. That goal was to increase the number of high quality scientists working on the breast cancer problem. Another very important measure of the success of your program is the fact that you have been able to continue the program by obtaining a training grant from the National Cancer Institute. I congratulate you and your colleagues on your accomplishments.

Sincerely,

Harold L. Moses, M.D.
B.F. Byrd, Jr. Professor of Oncology
Director, Vanderbilt Cancer Center
Professor and Chair, Department of Cell Biology

Date: Mon, 17 Aug 1998 11:11:34 -0700
From: Mina Bissell <mjbissell@lbl.gov>
Reply-To: mjbissell@lbl.gov
Organization: Lawrence Berkeley National Laboratory
MIME-Version: 1.0
To: "Maihle, Nita J., Ph.D." <maihle@mayo.edu>
Subject: "Biology of Breast Cancer"

Maihle, N.J.

Appendix N

Dear Nita:

I just discovered that I hadn't sent my very short write up of your program to you. I think in the confusion of a trip (I do a lot of work in the planes!), I must have left it behind. Here is even a shorter version of what I wrote:

The program in Biology of Breast Cancer is timely and competitive. The integration of basic and clinical research is ultimately what is needed in all these programs. The breadth of the background of the faculty is refreshing and would, if used properly, provide an appropriate base of knowledge for the trainees. The resources would be the envy of other national programs!

The curriculum, as stated, is excellent. The inclusion of developmental biology, principles of cell and tissue design and ethics as well as the more standard courses should be commended. However, it would have been helpful to have included the CV of the faculty and a history of their training students and fellows.

Sincerely,
Mina

Mina J. Bissell, Ph.D.
Director,
Life Sciences Division
Lawrence Berkeley National Laboratory
Content-Type: text/x-vcard; charset=us-ascii; name="vcard.vcf"
Content-Transfer-Encoding: 7bit
Content-Description: Card for Mina J. Bissell
Content-Disposition: attachment; filename="vcard.vcf"

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American Association for Cancer Education

Maihle, N.J.

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Appendix O

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Please follow format printed on reverse. The original typed copy of this ABSTRACT FORM (for photo-reproduction) and 10 photocopies must be submitted to:

Robert M. Chamberlain, Ph.D.
Dept. of Epidemiology, 189
M.D. Anderson Cancer Center
1515 Holcombe Blvd.
Houston, TX 77030
Phone: 713-792-7756
FAX: 713-792-0807

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No preference	<input type="checkbox"/>	

The text of your abstract must not touch this line

The Mayo Graduate School Biology of Breast Cancer Training Program Jeffrey L. Salisbury and Nita J. Maihle, Tumor Biology Program, Mayo Clinic, Rochester, MN 55905.

The Biology of Breast Cancer Training Program of the Mayo Clinic is a predoctoral training program in tumor biology. The focus of the program is to provide an educational environment that stimulates excellence in scientific thought and training while simultaneously providing exposure to all of the major fields of study relevant to tumor biology with a particular emphasis on breast and other women's cancers. The goals of the program are four-fold: First, to provide trainees with a solid and uniquely multidisciplinary knowledge base in the biology of cancer. Second, to guide the development of each individual trainee so that they achieve their fullest academic and research potential. Third, to aid trainees in establishment of their professional network of peers and colleagues in the field of cancer research. And, fourth, to stimulate new working alliances between students, fellows, and staff participating in cancer related research, education, and clinical endeavors at the Mayo Clinic and within the Mayo Cancer Center. Students participate in laboratory-based research, as well as in a formal tumor biology curriculum that integrates current concepts in cell growth control with the natural history of human tumors. The Biology of Breast Cancer Training Program courses establish a solid foundation in the biology of breast cancer and share several distinguishing features and innovative strategies for teaching which enhance learning and student/faculty participation. In particular, active involvement of students in the learning and discovery process, in information processing, and in the application of information to problems requires that students be accountable for learned information on an immediate and ongoing basis. Problem-centered learning also puts learning into context and facilitates learning transfer. These sessions allow students to organize and categorize information into meaningful units and to 'discover' novel relationships and extract and assimilate important points in an interactive and participatory manner. Supported by the US Army Medical Research and Materiel Command (DAMD17-94-J-4116) and the Mayo Clinic Foundation.

The text of your abstract must not touch this line

Type font preferred: New Times Roman 12 point • Justification on right and left is preferred

Abstract to be presented by:

Jeffrey L. Salisbury, Ph.D.

(Type name of PRESENTER)

Gugg-14, Mayo Clinic, Rochester, MN 55905

(address)

(city and state, ZIP code, country)

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As the 1st AUTHOR of this abstract, on behalf of all the authors, I hereby transfer its copyright to the American Association for Cancer Education

Signature of 1st Author

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